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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12N 15/31, C07K 14/315, A61K 39/09, C12N 1/21	A2	(11) International Publication Number: WO 99/42588 (43) International Publication Date: 26 August 1999 (26.08.99)
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(54) Title: GROUP B STREPTOCOCCUS ANTIGENS (57) Abstract Group B streptococcus (GBS) proteins and polynucleotides encoding them are disclosed. Said proteins are antigenic and therefore useful vaccine components for the prophylaxis or therapy of streptococcus infection in animals. Also disclosed are recombinant methods of producing the protein antigens as well as diagnostic assays for detecting streptococcus bacterial infection.		

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GROUP B STREPTOCOCCUS ANTIGENS

5

FIELD OF THE INVENTION

The present invention is related to antigens, more particularly protein antigens of group B streptococcus (GBS) bacterial pathogen which are useful as vaccine components for therapy and/or prophylaxis.

15

BACKGROUND OF THE INVENTION

Streptococcus are gram (+) bacteria that are differentiated by group specific carbohydrate antigens A through O found on their cell surface. Streptococcus groups are further distinguished by type-specific capsular polysaccharide antigens. Several serotypes have been identified for the Group B streptococcus (GBS) : Ia, Ib, II, III, IV, V, VI, VII and VIII. GBS also contains antigenic proteins known as "C-proteins" (alpha, beta, gamma and delta), some of which have been cloned.

25

Although GBS is a common component of the normal human vaginal and colonic flora this pathogen has long been recognized as a major cause of neonatal sepsis and meningitis, late-onset meningitis in infants, postpartum endometritis as well as mastitis in dairy herds. Expectant mothers exposed to GBS are at risk of postpartum infection and may transfer the infection to their baby as the child passes through the birth canal. Although the organism is sensitive to antibiotics, the high attack rate and rapid onset of sepsis in neonates and meningitis in infants results in high morbidity and mortality.

To find a vaccine that will protect individuals from GBS infection, researches have turned to the type-specific antigens. Unfortunately these polysaccharides have proven to
5 be poorly immunogenic in humans and are restricted to the particular serotype from which the polysaccharide originates. Further, capsular polysaccharide elicit a T cell independent response i.e. no IgG production. Consequently capsular polysaccharide antigens are unsuitable
10 as a vaccine component for protection against GBS infection.

Others have focused on the C-protein beta antigen which demonstrated immunogenic properties in mice and rabbit models. This protein was found to be unsuitable as a human
15 vaccine because of its undesirable property of interacting with high affinity and in a non-immunogenic manner with the Fc region of human IgA. The C-protein alpha antigen is rare in type III serotypes of GBS which is the serotype responsible for most GBS mediated conditions and is
20 therefore of little use as a vaccine component.

Therefore there remains an unmet need for GBS antigens that may be used as vaccine components for the prophylaxis and/or
25 therapy of GBS infection.

SUMMARY OF THE INVENTION

30 According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence selected from the group consisting of:
SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
35 SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO:10,
SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15,
SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19,

SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24,
SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29,
SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34,
SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39,
5 SEQ ID NO:40, SEQ ID NO:41 and SEQ ID NO:44 or fragments,
analogs or derivatives thereof.

In other aspects, there is provided vectors comprising
polynucleotides of the invention operably linked to an
10 expression control region, as well as host cells transfected
with said vectors and methods of producing polypeptides
comprising culturing said host cells under conditions
suitable for expression.

15 In yet another aspect, there is provided novel polypeptides
encoded by polynucleotides of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

20

Figure 1a is the DNA sequence of clone 1 (SEQ ID NO :1) with
corresponding amino acid sequences for open reading frames;
figure 1b is the amino acid sequence SEQ ID NO: 2;
figure 1c is the amino acid sequence SEQ ID NO: 3;
25 figure 1d is the amino acid sequence SEQ ID NO: 4;
figure 1e is the amino acid sequence SEQ ID NO: 5;
figure 1f is the amino acid sequence SEQ ID NO: 6;

Figure 2a is the DNA sequence of clone 2 (SEQ ID NO :7) with
30 corresponding amino acid sequences for open reading frames;
figure 2b is the amino acid sequence SEQ ID NO: 8;
figure 2c is the amino acid sequence SEQ ID NO: 9;
figure 2d is the amino acid sequence SEQ ID NO:10;
figure 2e is the amino acid sequence SEQ ID NO:11;
35 figure 2f is the amino acid sequence SEQ ID NO:12;

Figure 3a is the DNA sequence of clone 3 (SEQ ID NO :13)
with corresponding amino acid sequences for open reading
frames;

figure 3b is the amino acid sequence SEQ ID NO:14;

5 figure 3c is the amino acid sequence SEQ ID NO:15;

figure 3d is the amino acid sequence SEQ ID NO:16;

figure 3e is the amino acid sequence SEQ ID NO:17;

figure 3f is the amino acid sequence SEQ ID NO:18;

figure 3g is the amino acid sequence SEQ ID NO:19;

10 figure 3h is the amino acid sequence SEQ ID NO:20;

figure 3i is the amino acid sequence SEQ ID NO:21;

Figure 4a is the DNA sequence of clone 4 (SEQ ID NO :22)
with corresponding amino acid sequences for open reading
15 frames;

figure 4b is the amino acid sequence SEQ ID NO:23;

figure 4c is the amino acid sequence SEQ ID NO:24;

figure 4d is the amino acid sequence SEQ ID NO:25;

20 figure 4e is the amino acid sequence SEQ ID NO:26;

Figure 5a is the DNA sequence of clone 5 (SEQ ID NO :27)
with corresponding amino acid sequences for open reading
frames;

figure 5b is the amino acid sequence SEQ ID NO:28;

25 figure 5c is the amino acid sequence SEQ ID NO:29;

figure 5d is the amino acid sequence SEQ ID NO:30;

figure 5e is the amino acid sequence SEQ ID NO:31;

Figure 6a is the DNA sequence of clone 6 (SEQ ID NO :32) ;

30 figure 6b is the amino acid sequence SEQ ID NO:33;

figure 6c is the amino acid sequence SEQ ID NO:34;

figure 6d is the amino acid sequence SEQ ID NO:35;

figure 6e is the amino acid sequence SEQ ID NO:36;

35 Figure 7a is the DNA sequence of clone 7 (SEQ ID NO :37);

figure 7b is the amino acid sequence SEQ ID NO:38;

figure 7c is the amino acid sequence SEQ ID NO:39;

figure 7d is the amino acid sequence SEQ ID NO:40;

figure 7e is the amino acid sequence SEQ ID NO:41;

- 5 Figure 8 is the DNA sequence of a part of clone 7 including a signal sequence (SEQ ID NO :42);

Figure 9 is the DNA sequence of a part of clone 7 without a signal sequence (SEQ ID NO :43);

- 10 Figure 9a is the amino acid sequence (SEQ ID NO:44);

Figure 10 represents the distribution of anti-GBS ELISA titers in sera from CD-1 mice immunized with recombinant GBS protein corresponding to the SEQ ID NO:39.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to novel antigenic polypeptides of group B streptococcus (GBS) characterized by the amino acid sequence selected from the group consisting of:

SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO:10,
SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15,
10 SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19,
SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24,
SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29,
SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34,
SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39,
15 SEQ ID NO:40, SEQ ID NO:41 and SEQ ID NO:44 or fragments,
analogues or derivatives thereof.

A preferred embodiment of the invention includes SEQ ID NO :39 and SEQ ID NO:44.

20

A further preferred embodiment of the invention is SEQ ID NO :39.

A further preferred embodiment of the invention is SEQ ID NO :44.

25

As used herein, "fragments", "derivatives" or "analogues" of the polypeptides of the invention include those polypeptides in which one or more of the amino acid residues are substituted with a conserved or non-conserved amino acid residue (preferably conserved) and which may be natural or unnatural.

30

The terms «fragments», «derivatives» or «analogues» of polypeptides of the present invention also include polypeptides which are modified by addition, deletion,

35

substitution of amino acids provided that the polypeptides retain the capacity to induce an immune response.

5 By the term «conserved amino acid» is meant a substitution of one or more amino acids for another in which the antigenic determinant (including its secondary structure and hydropathic nature) of a given antigen is completely or partially conserved in spite of the substitution.

10 For example, one or more amino acid residues within the sequence can be substituted by another amino acid of a similar polarity, which acts as a functional equivalent, resulting in a silent alteration. Substitutes for an amino acid within the sequence may be selected from other members
15 of the class to which the amino acid belongs. For example, the nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. The polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine,
20 asparagine and glutamine. The positively charged (basic) amino acids include arginine, lysine and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid.

25 Preferably, derivatives and analogs of polypeptides of the invention will have about 70% identity with those sequences illustrated in the figures or fragments thereof. That is, 70% of the residues are the same. More preferably polypeptides will have greater than 95% homology. In another
30 preferred embodiment, derivatives and analogs of polypeptides of the invention will have fewer than about 20 amino acid residue substitutions, modifications or deletions and more preferably less than 10. Preferred substitutions are those known in the art as conserved i.e. the substituted
35 residues share physical or chemical properties such as hydrophobicity, size, charge or functional groups.

Furthermore, in those situations where amino acid regions are found to be polymorphic, it may be desirable to vary one or more particular amino acids to more effectively mimic the
5 different epitopes of the different GBS strains.

Also included are polypeptides which have fused thereto other compounds which alter the polypeptides biological or pharmacological properties i.e. polyethylene glycol (PEG) to
10 increase half-life; leader or secretory amino acid sequences for ease of purification; prepro- and pro- sequences; and (poly)saccharides.

Moreover, the polypeptides of the present invention can be
15 modified by terminal -NH₂ acylation (eg. by acetylation, or thioglycolic acid amidation, terminal carbosy amidation, e.g. with ammonia or methylamine) to provide stability, increased hydrophobicity for linking or binding to a support or other molecule.

20 Also contemplated are hetero and homo polypeptide multimers of the polypeptide fragments, analogues and derivatives. These polymeric forms include, for example, one or more polypeptides that have been cross-linked with cross-linkers
25 such as avidin/biotin, gluteraldehyde or dimethyl-superimide. Such polymeric forms also include polypeptides containing two or more tandem or inverted contiguous sequences, produced from multicistronic mRNAs generated by recombinant DNA technology.

30 Preferably, a fragment, analog or derivative of a polypeptide of the invention will comprise at least one antigenic region i.e. at least one epitope.

In order to achieve the formation of antigenic polymers
35 (i.e. synthetic multimers), polypeptides may be utilized having bishaloacetyl groups, nitroarylhalides, or the like,

where the reagents being specific for thio groups.
Therefore, the link between two mercapto groups of the
different peptides may be a single bond or may be composed
of a linking group of at least two, typically at least four,
5 and not more than 16, but usually not more than about 14
carbon atoms.

In a particular embodiment, polypeptide fragments, analogs
and derivatives of the invention do not contain a methionine
10 (Met) starting residue. Preferably, polypeptides will not
incorporate a leader or secretory sequence (signal
sequence). The signal portion of a polypeptide of the
invention may be determined according to established
molecular biological techniques. In general, the
15 polypeptide of interest may be isolated from a GBS culture
and subsequently sequenced to determine the initial residue
of the mature protein and therefor the sequence of the
mature polypeptide.

20 According to another aspect, there is provided vaccine
compositions comprising one or more GBS polypeptides of the
invention in admixture with a pharmaceutically acceptable
carrier diluent or adjuvant.

25 Suitable adjuvants include oils i.e. Freund's complete or
incomplete adjuvant; salts i.e. $\text{AlK}(\text{SO}_4)_2$, $\text{AlNa}(\text{SO}_4)_2$,
 $\text{AlNH}_4(\text{SO}_4)_2$, $\text{Al}(\text{OH})_3$, AlPO_4 , silica, kaolin; saponin
derivative; carbon polynucleotides i.e. poly IC and poly AU
and also detoxified cholera toxin (CTB) and E.coli heat
30 labile toxin for induction of mucosal immunity. Preferred
adjuvants include QuilATM, AlhydrogelTM and AdjuphosTM.
Vaccines of the invention may be administered parenterally
by injection, rapid infusion, nasopharyngeal absorption,
dermoabsorption, or bucal or oral.

35

- Vaccine compositions of the invention are used for the treatment or prophylaxis of *streptococcus* infection and/or diseases and symptoms mediated by *streptococcus* infection, in particular group A *streptococcus* (*pyogenes*), group B *streptococcus* (GBS or *agalactiae*), *dysgalactiae*, *uberis*, *nocardia* as well as *Staphylococcus aureus*. General information about *Streptococcus* is available in Manual of Clinical Microbiology by P.R.Murray et al. (1995, 6th Edition, ASM Press, Washington, D.C.). More particularly group B *streptococcus*, *agalactiae*. In a particular embodiment vaccines are administered to those individuals at risk of GBS infection such as pregnant women and infants for sepsis, meningitis and pneumonia as well as immunocompromised individuals such as those with diabetes, liver disease or cancer. Vaccines may also have veterinary applications such as for the treatment of mastitis in cattle which is mediated by the above mentioned bacteria as well as *E.coli*.
- 20 The vaccine of the present invention can also be used for the manufacture of a medicament used for the treatment or prophylaxis of *streptococcus* infection and/or diseases and symptoms mediated by *streptococcus* infection, in particular group A *streptococcus* (*pyogenes*), group B *streptococcus* (GBS or *agalactiae*), *dysgalactiae*, *uberis*, *nocardia* as well as *Staphylococcus aureus*. More particularly group B *streptococcus*, *agalactiae*.

- Vaccine compositions are preferably in unit dosage form of about 0.001 to 100 µg/kg (antigen/body weight) and more preferably 0.01 to 10 µg/kg and most preferably 0.1 to 1 µg/kg 1 to 3 times with an interval of about 1 to 12 weeks intervals between immunizations, and more preferably 1 to 6

weeks.

According to another aspect, there is provided polynucleotides encoding polypeptides of group B

5 streptococcus (GBS) characterized by the amino acid sequence selected from the group consisting of:

SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
 SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO:10,
 SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15,
 10 SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19,
 SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24,
 SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29,
 SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34,
 SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39,
 15 SEQ ID NO:40, SEQ ID NO:41 and SEQ ID NO:44 or fragments,
 analogs or derivatives thereof.

Preferred polynucleotides are those illustrated in figures 1a (SEQ ID NO: 1), 2a (SEQ ID NO: 7), 3a (SEQ ID NO: 13), 4a

20 (SEQ ID NO: 22), 5a (SEQ ID NO: 27), 6a (SEQ ID NO: 32), 7a (SEQ ID NO: 37), 8 (SEQ ID NO : 42) and 9 (SEQ ID NO : 43) which correspond to the open reading frames, encoding polypeptides of the invention.

25 Preferred polynucleotides are those illustrated in figures 1a (SEQ ID NO: 1), 2a (SEQ ID NO: 7), 3a (SEQ ID NO: 13), 4a (SEQ ID NO: 22), 5a (SEQ ID NO: 27), 6a (SEQ ID NO: 32), 7a (SEQ ID NO: 37), 8 (SEQ ID NO : 42) and 9 (SEQ ID NO : 43) and fragments, analogues and derivatives thereof.

30 More preferred polynucleotides of the invention are those illustrated in Figures 7 (SEQ ID NO : 37), 8 (SEQ ID NO : 42) and 9 (SEQ ID NO : 43).

35 Most preferred polynucleotides of the invention are those illustrated in Figures 8 (SEQ ID NO : 42) and 9 (SEQ ID NO :

43) .

It will be appreciated that the polynucleotide sequences illustrated in the figures may be altered with degenerate
5 codons yet still encode the polypeptides of the invention.

Due to the degeneracy of nucleotide coding sequences, other polynucleotide sequences which encode for substantially the same polypeptides of the present invention may be used in
10 the practice of the present invention. These include but are not limited to nucleotide sequences which are altered by the substitution of different codons that encode the same amino acid residue within the sequence, thus producing a silent change.

15 Accordingly the present invention further provides polynucleotides which hybridize to the polynucleotide sequences herein above described (or the complement sequences thereof) having 50% and preferably at least 70%
20 identity between sequences. More preferably polynucleotides are hybridizable under stringent conditions i.e. having at least 95% identity and most preferably more than 97% identity.

25 By capable of hybridizing under stringent conditions is meant annealing of a nucleic acid molecule to at least a region of a second nucleic acid sequence (whether as cDNA, mRNA, or genomic DNA) or to its complementary strand under standard conditions, e.g. high temperature and/or low salt
30 content, which tend to disfavor hybridization of noncomplementary nucleotide sequences. A suitable protocol is described in Maniatis T. et al., Molecular cloning : A Laboratory Manual, Cold Springs Harbor Laboratory, 1982, which is herein incorporated by reference.

35 In a further aspect, polynucleotides encoding polypeptides

of the invention, or fragments, analogs or derivatives thereof, may be used in a DNA immunization method. That is, they can be incorporated into a vector which is replicable and expressible upon injection thereby producing
5 the antigenic polypeptide in vivo. For example polynucleotides may be incorporated into a plasmid vector under the control of the CMV promoter which is functional in eukaryotic cells. Preferably the vector is injected intramuscularly.

10

According to another aspect, there is provided a process for producing polypeptides of the invention by recombinant techniques by expressing a polynucleotide encoding said polypeptide in a host cell and recovering the expressed
15 polypeptide product. Alternatively, the polypeptides can be produced according to established synthetic chemical techniques i.e. solution phase or solid phase synthesis of oligopeptides which are ligated to produce the full polypeptide (block ligation).

20

For recombinant production, host cells are transfected with vectors which encode the polypeptide, and then cultured in a nutrient media modified as appropriate for activating promoters, selecting transformants or amplifying the genes.
25 Suitable vectors are those that are viable and replicable in the chosen host and include chromosomal, non-chromosomal and synthetic DNA sequences e.g. bacterial plasmids, phage DNA, baculovirus, yeast plasmids, vectors derived from combinations of plasmids and phage DNA. The polypeptide
30 sequence may be incorporated in the vector at the appropriate site using restriction enzymes such that it is operably linked to an expression control region comprising a promoter, ribosome binding site (consensus region or Shine-Dalgarno sequence), and optionally an operator (control
35 element). One can select individual components of the expression control region that are appropriate for a given

host and vector according to established molecular biology principles (Sambrook et al, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor, N.Y., 1989 incorporated herein by reference). Suitable promoters include but are not
5 limited to LTR or SV40 promoter, *E.coli* lac, tac or trp promoters and the phage lambda P_L promoter. Vectors will preferably incorporate an origin of replication as well as selection markers i.e. ampicillin resistance gene. Suitable bacterial vectors include pET, pQE70, pQE60, pQE-9, pbs,
10 pD10 phagescript, psiX174, pbluescript SK, pbsks, pNH8A, pNH16a, pNH18A, pNH46A, ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 and eukaryotic vectors pBlueBacIII, pWLNEO, pSV2CAT, pOG44, pXT1, pSG, pSVK3, pBPV, pMSG and pSVL. Host cells may be bacterial i.e. *E.coli*, *Bacillus subtilis*,
15 *Streptomyces*; fungal i.e. *Aspergillus niger*, *Aspergillus nidulins*; yeast i.e. *Saccharomyces* or eukaryotic i.e. CHO, COS.

Upon expression of the polypeptide in culture, cells are
20 typically harvested by centrifugation then disrupted by physical or chemical means (if the expressed polypeptide is not secreted into the media) and the resulting crude extract retained to isolate the polypeptide of interest. .
Purification of the polypeptide from culture media or lysate
25 may be achieved by established techniques depending on the properties of the polypeptide i.e. using ammonium sulfate or ethanol precipitation , acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, hydroxylapatite
30 chromatography and lectin chromatography. Final purification may be achieved using HPLC.

The polypeptide may be expressed with or without a leader or secretion sequence. In the former case the leader may be
35 removed using post-translational processing (see US

4,431,739; 4,425,437; and 4,338,397 incorporated herein by reference) or be chemically removed subsequent to purifying the expressed polypeptide.

- 5 According to a further aspect, the GBS polypeptides of the invention may be used in a diagnostic test for streptococcus infection in particular GBS infection. Several diagnostic methods are possible, for example detecting streptococcus organism in a biological sample, the following procedure may
10 be followed:
- a) obtaining a biological sample from a patient;
 - b) incubating an antibody or fragment thereof reactive with a GBS polypeptide of the invention with the biological sample to form a mixture; and
 - 15 c) detecting specifically bound antibody or bound fragment in the mixture which indicates the presence of streptococcus.

- Alternatively, a method for the detection of antibody
20 specific to a streptococcus antigen in a biological sample containing or suspected of containing said antibody may be performed as follows:
- a) isolating a biological sample from a patient;
 - b) incubating one or more GBS polypeptides of the
25 invention or fragments thereof with the biological sample to form a mixture; and
 - c) detecting specifically bound antigen or bound fragment in the mixture which indicates the presence of antibody specific to streptococcus.

- 30 One of skill in the art will recognize that this diagnostic test may take several forms, including an immunological test such as an enzyme-linked immunosorbent assay (ELISA), a radioimmunoassay or a latex agglutination assay, essentially
35 to determine whether antibodies specific for the protein are present in an organism.

The DNA sequences encoding polypeptides of the invention may also be used to design DNA probes for use in detecting the presence of streptococcus in a biological sample suspected of containing such bacteria. The detection method of this invention comprises:

- a) isolating the biological sample from a patient;
- b) incubating one or more DNA probes having a DNA sequence encoding a polypeptide of the invention or fragments thereof with the biological sample to form a mixture; and
- c) detecting specifically bound DNA probe in the mixture which indicates the presence of streptococcus bacteria.

The DNA probes of this invention may also be used for detecting circulating streptococcus i.e. GBS nucleic acids in a sample, for example using a polymerase chain reaction, as a method of diagnosing streptococcus infections. The probe may be synthesized using conventional techniques and may be immobilized on a solid phase, or may be labeled with a detectable label. A preferred DNA probe for this application is an oligomer having a sequence complementary to at least about 6 contiguous nucleotides of the GBS polypeptides of the invention.

Another diagnostic method for the detection of streptococcus in a patient comprises:

- a) labeling an antibody reactive with a polypeptide of the invention or fragment thereof with a detectable label;
- b) administering the labeled antibody or labeled fragment to the patient; and
- c) detecting specifically bound labeled antibody or labeled fragment in the patient which indicates the presence of streptococcus.

A further aspect of the invention is the use of the GBS

polypeptides of the invention as immunogens for the production of specific antibodies for the diagnosis and in particular the treatment of streptococcus infection. Suitable antibodies may be determined using appropriate screening methods, for example by measuring the ability of a particular antibody to passively protect against streptococcus infection in a test model. One example of an animal model is the mouse model described in the examples herein. The antibody may be a whole antibody or an antigen-binding fragment thereof and may in general belong to any immunoglobulin class. The antibody or fragment may be of animal origin, specifically of mammalian origin and more specifically of murine, rat or human origin. It may be a natural antibody or a fragment thereof, or if desired, a recombinant antibody or antibody fragment. The term recombinant antibody or antibody fragment means antibody or antibody fragment which were produced using molecular biology techniques. The antibody or antibody fragments may be polyclonal, or preferably monoclonal. It may be specific for a number of epitopes associated with the GBS polypeptides but is preferably specific for one.

EXAMPLE 1 Murine model of lethal Group B Streptococcus (GBS) infection

The mouse model of GBS infection is described in detail in Lancefield et al (J Exp Med 142:165-179,1975). GBS strain C388/90 (Clinical isolate obtained in 1990 from the cephalorachidian fluid of a patient suffering from meningitis, Children's Hospital of Eastern Ontario, Ottawa, Canada) and NCS246 (National Center for Streptococcus, Provincial Laboratory of Public Health for Northern Alberta, Edmonton, Canada) were respectively serotyped as type Ia/c and type II/R.

To increase their virulence, the GBS strains C388/90 (serotype Ia/c) and NCS 246 (serotype II/R) were serially passaged through mice as described previously (Lancefield et al. J Exp Med 142:165-179, 1975). Briefly, the increase of virulence was monitored using intraperitoneal inoculations of serial dilutions of a subculture in Todd-Hewitt broth obtained from either the blood or spleen of infected mice. After the last passage, infected blood samples were used to inoculate Todd-Hewitt broth. After an incubation of 2 hours at 37°C with 7% CO₂, glycerol at a final concentration of 10% (v/v) was added to the culture. The culture was then aliquoted and stored at -80° C for use in GBS challenge experiments. The number of cfu of GBS present in these frozen samples was determined. The bacterial concentration necessary to kill 100% (LD100) of the 18 weeks old mice were determined to be 3.5X10⁵ and 1.1X10⁵ respectively for GBS strain C388/90 and NCS246, which corresponded to a significant increase in virulence for both strains. Indeed, the LD100 recorded before the passages for these two strains was higher than 10⁹ cfu.

In a bacterial challenge, a freshly thawed aliquot of a virulent GBS strain was adjusted to the appropriate bacterial concentration using Todd-Hewitt broth and 1ml was injected intraperitoneally to each female CD-1 mouse. The mice used for the passive protection experiments were 6 to 8 weeks old, while the ones used for the active protection experiments were approximately 18 weeks old at the time of the challenge. All inocula were verified by colony counts. Animals were observed for any sign of infection four times daily for the first 48 h after challenge and then daily for the next 12 days. At the end of that period, blood samples were obtained from the survivors and frozen at -20°C. The spleen obtained from each mouse that survived the challenge was cultured in order to identify any remaining GBS.

EXAMPLE 2 Immunization and protection in mice with formaldehyde killed whole GBS cells

- 5 Formaldehyde killed GBS whole cells were prepared according to the procedures described in Lancefield et al (J Exp Med 142:165-179,1975). Briefly, an overnight culture on sheep blood agar plates (Quelab Laboratories, Montreal, Canada) of a GBS strain was washed twice in PBS buffer (phosphate buffered-saline, pH7.2), adjusted to approximately 3×10^9 cfu/mL and incubated overnight in PBS containing 0.3% (v/v) formaldehyde. The killed GBS suspension was washed with PBS and kept frozen at -80°C .
- 15 Female CD-1 mice, 6 to 8 weeks old (Charles River, St-Constant, Québec, Canada), were injected subcutaneously three times at two weeks interval with 0.1 ml of formaldehyde killed cells of GBS strain C388/90 ($\sim 6 \times 10^7$ GBS), or 0.1 ml of PBS for the control group. On the day before
- 20 the immunization, Alhydrogel™ (Superfos Biosector, Frederikssund, Denmark) at a final concentration of 0.14 mg or 0.21 mg of Al, was added to these preparations and incubated overnight at 4°C with agitation. Serum samples were obtained from each mouse before the beginning of the
- 25 immunization protocol and two weeks after the last injection. The sera were frozen at -20°C .

- Eight mice in each control group injected with PBS and the group immunized with formaldehyde killed whole cells GBS strain C388/90 (Ia/c) were challenged with 1.5×10^4 cfu of GBS strain C388/90 (Ia/c) one week after the third injection. All mice immunized with the formaldehyde killed GBS whole cells survived the homologous challenge while, within 5 days after the challenge, only 4 out of the 8 mice
- 35 injected with PBS survived from the infection. In order to increase the mortality rate in the control groups, the

bacterial suspension had to be adjusted according to the age of the mice at the time of the bacterial challenge. In subsequent challenge experiments, when mice were older than 15 weeks, the bacterial inoculum was increased to
5 concentrations between 3.0×10^5 and 2.5×10^6 cfu.

Table 1 Immunization of CD1 mice with formaldehyde killed whole cells of GBS and subsequent homologous challenge [strain C388/90 (Ia/c)] and heterologous challenge [strain NCS246 (II/R)].

antigenic preparations used for immunization ¹	number of living mice 14 days after the bacterial challenge (% Survival)	
	homologous challenge: strain C388/90 (Ia/c)	heterologous challenge: strain NCS246 (II/R)
1st infection		
formaldehyde killed cells of GBS strain C388/90 (Ia/c) ²	8/8 (100) ³	n.d. ⁵
control PBS	4/8 (50)	n.d.
2nd infection		
formaldehyde killed cells of GBS strain C388/90 (Ia/c)	6/6 (100) ⁴	0/6 (0) ⁶
control PBS	2/6 (33)	0/6 (0)

¹ alhydrogel™ at a final concentration of 0.14 mg or 0.21mg of Al was used;

² approximately 6×10^7 cfu;

³ intraperitoneal challenge with 1 mL Todd-Hewitt culture medium containing GBS C388/90 (Ia/c) suspension adjusted to 1.5×10^4 cfu;

⁴ intraperitoneal challenge with 1 mL Todd-Hewitt culture medium containing GBS C388/90 (Ia/c) suspension adjusted to 2.1×10^6 cfu;

⁵ not done;

⁶ intraperitoneal challenge with 1 mL Todd-Hewitt culture medium containing GBS NCS246 (II/R) suspension adjusted to 1.2×10^5 cfu.

In another experiment, one group of 12 mice corresponding to a control group was injected with PBS, while a second group of 12 mice was immunized with formaldehyde killed whole cells of GBS strain C388/90 (Ia/c). Six mice from each of these two groups were challenged with 2.1×10^6 cfu of the GBS strain C388/90 (Ia/c) (Table I). As the first challenge experiment, all mice immunized with the GBS strain C388/90 (Ia/c) survived the homologous challenge. Only two out of the 6 mice injected with PBS survived the infection.

The remaining 6 mice in both groups were then used one week later to verify whether this antigenic preparation could confer cross protection against strain NCS246 (II/R) which produce a serologically distinct capsule. None of the mice infected with this second GBS strain survived the infection. The later result suggested that most of the protective immune response induced by formaldehyde killed strain C388/90 is directed against the capsular polysaccharide and that it could be restricted to strains of that particular serotype. These results clearly indicated that this particular model of infection can be efficiently used to study the protection conferred by vaccination.

15

EXAMPLE 3 Immunization of rabbit with formaldehyde killed whole GBS cells and passive protection in mice

A New Zealand rabbit (2.5 kg, Charles River, St-Constant, Québec, Canada) was immunized with formaldehyde killed cells of GBS strain C388/90 (Ia/c) to obtain hyperimmune serum. This rabbit was injected subcutaneously three times at three weeks interval with approximately 1.5×10^9 cfu of formaldehyde killed whole cells of GBS strain C388/90 (Ia/c). Freund's complete adjuvant (Gibco BRL Life Technologies, Grand Island, New York) was used as the adjuvant for the first immunization, while Freund's incomplete adjuvant (Gibco BRL) was used for the following two injections. Serum samples were obtained before the beginning of the immunization protocol and two weeks after the last injection. The sera were frozen at -20°C .

The ability of this particular rabbit hyperimmune serum to passively protect mice against a lethal infection with GBS

was also evaluated. Intraperitoneal injection of mice with either 15 or 25 μ L of hyperimmune rabbit serum 18 hours before the challenge protected 4 out of 5 mice (80%) against the infection. Comparatively, survival rates lower than 20% were recorded for mice in the control group injected with PBS or serum obtained from a rabbit immunized with meningococcal outer membrane preparation. This result clearly indicates that the immunization of another animal species with killed GBS cells can induce the production of antibodies that can passively protect mice. This reagent will also be used to characterize clones.

Table 2 Passive protection of CD-1 mice conferred by rabbit serum obtained after immunization with formaldehyde killed group B whole streptococci (strain C388/90 (Ia/c)) antigenic preparation

groups	number of living mice 14 days after the bacterial challenge with GBS strain C388/90 (Ia/c) ²	% survival
rabbit hyperimmune serum ² - 25 μ l	4/5	80
rabbit hyperimmune serum ¹ - 15 μ l	4/5	80
control rabbit serum - 25 μ l	1/5	20
control PBS	1/10	10

¹ Freund's complete adjuvant was used for first immunization, and Freund's incomplete adjuvant for the following two injections;

² intraperitoneal challenge with 1 ml Todd-Hewitt culture medium containing GBS C388/90 (Ia/c) suspension adjusted to 2×10^4 cfu.

EXAMPLE 4 Recombinant production of His.Tag-GBS fusion protein

The coding region of a GBS gene was amplified by PCR (DNA Thermal Cyclor GeneAmp PCR system 2400 Perkin Elmer, San Jose, CA) from the genomic DNA of GBS strain C388/90 (Ia/c) using the oligos that contained base extensions for the addition of the restriction sites BglII (AGATCT) and HindIII (AAGCTT), respectively. The PCR product was purified from agarose gel using a Qiaex II gel extraction kit from Qiagen (Chatsworth, CA), digested with the restriction enzymes BglII and HindIII (Pharmacia Canada Inc Baie d'Urfe, Canada), and extracted with phenol:chloroform before ethanol precipitation. The pET-32b(+) vector (Novagen, Madison, WI) containing the thioredoxin-His.Tag sequence was digested with the restriction enzymes BglII and HindIII, extracted with phenol:chloroform, and then ethanol precipitated. The BglII-HindIII genomic DNA fragment was ligated to the BglII-HindIII pET-32b(+) vector to create the coding sequence for thioredoxin-His.Tag-GBS fusion protein whose gene was under control of the T7 promoter. The ligated products were transformed into *E. coli* strain XLI Blue MRF' ($\Delta(mcrA)183\Delta(mcrCB-hsdSMR-mrr)173$ *endA1 supE44 thi-1 recA1 gyrA96 relA1 lac* [F'proAB *lacI*^qZAM15Tn10 (Tet^r)]^c) (Stratagene, La Jolla, CA) according to the method of Simanis (Hanahan, D. DNA Cloning, 1985, D.M. Glover (ed.), pp. 109-135). The recombinant pET plasmid was purified using a Qiagen kit (Qiagen, Chatsworth, CA) and the nucleotide sequence of the DNA insert was verified by DNA sequencing (Taq Dye Deoxy Terminator Cycle Sequencing kit, ABI, Foster City, CA). The recombinant pET plasmid was transformed by electroporation (Gene Pulser II apparatus, BIO-RAD Labs, Mississauga, Canada) into *E. coli* strain AD494 (DE3) ($\Delta ara^+ leu7697 \Delta lacX74 \Delta phoA PvuII phoR \Delta malF3$ F'[*lac*'(*lacI*^q) *pro*] *trxB::Kan* (DE3)) (Novagen, Madison, WI). In this strain of

E. coli, the T7 promoter controlling expression of the fusion protein, is specifically recognized by the T7 RNA polymerase (present on the λ DE3 prophage) whose gene is under the control of the lac promoter which is inducible by isopropyl- β -D-thio-galactopyranoside (IPTG).

The transformant AD494(DE3)/rpET was grown at 37°C with agitation at 250 rpm in LB broth (peptone 10g/L, Yeast extract 5g/L, NaCl 10g/L) containing 100 μ g of ampicillin (Sigma-Aldrich Canada Ltd., Oakville, Canada) per mL until the A_{600} reached a value of 0.6. In order to induce the production of the thioredoxin-His.Tag-GBS fusion protein, the cells were incubated for 2 additional hours in the presence of IPTG at a final concentration of 1mM. The bacterial cells were harvested by centrifugation.

The recombinant fusion protein produced by AD494(DE3)/rpET32 upon IPTG induction for 2h was partially obtained as insoluble inclusion bodies which were purified from endogenous *E. coli* proteins by the isolation of insoluble aggregates (Gerlach, G.F. et al 1992, Infect. Immun. 60:892). Induced cells from a 500 mL culture were resuspended in 20 mL of 25% sucrose-50mM Tris-HCl buffer (pH8.0) and frozen at -70°C. Lysis of cells in thawed suspension was achieved by the addition of 5mL of a solution of lysozyme (10mg/mL) in 250mM Tris-HCl buffer (pH8.0) followed by an incubation of 10 to 15 min on ice, and the addition of 150mL of detergent mix (5 parts of 20mM Tris-HCl buffer [pH7.4]-300mM NaCl-2% deoxycholic acid-2% Nonidet P-40 and 4 parts of 100mM Tris-HCl buffer [pH8]-50mM EDTA-2% Triton X-100) followed by 5 min incubation on ice. Upon sonication, protein aggregates were harvested by centrifugation for 30 min at 35,000 X g and a sample of the soluble cellular fraction was kept. The aggregated proteins were solubilized in 6M guanidine hydrochloride. The

presence of the fusion protein in both the soluble and insoluble fractions was shown by Western Blot analysis using the serum of a mouse injected with formaldehyde killed cells of GBS strain C388/90 (Ia/c) that survived a bacterial
5 challenge with the corresponding GBS strain.

The purification of the fusion protein from the soluble fraction of IPTG-induced AD494(DE3)/rpET was done by affinity chromatography based on the properties of the
10 His.Tag sequence (6 consecutive histidine residues) to bind to divalent cations (Ni^{2+}) immobilized on the His.Bind metal chelation resin (Novagen, Madison, WI). The purification method used are those described in the pET system Manual, 6th Edition (Novagen, Madison, WI). Briefly, the pelleted
15 cells obtained from a 100mL culture induced with IPTG was resuspended in 4mL of Binding buffer (5mM imidazole-500mM NaCl-20mM Tris-HCl pH7.9), sonicated, and spun at 39,000 X g for 20 min to remove debris. The supernatant was filtered (0.45 μ m pore size membrane) and deposited on a column of
20 His.Bind resin equilibrated in Binding buffer. The column was then washed with 10 column volumes of Binding buffer followed by 6 column volumes of Wash buffer (20mM imidazole-500mM NaCl-20mM Tris-HCl pH7.9). The thioredoxin-His.Tag-GBS fusion protein was eluted with Elute buffer (1M
25 imidazole-500mM NaCl-20mM Tris-HCl pH7.9). The removal of the salt and imidazole from the sample was done by dialysis against 3 X 1 liter PBS at 4°C.

The quantities of fusion protein obtained from either the
30 soluble or insoluble cytoplasmic fractions of *E. coli* were estimated by Coomassie staining of a sodium dodecyl sulfate (SDS)-polyacrylamide gel with serial dilutions of these proteins and a bovine serum albumin standard (Pierce Chemical Co. Rockford, Ill.).

35

EXAMPLE 5 Recombinant production of GBS protein under
control of lambda P_L promoter

The DNA coding region of a GBS protein was inserted
5 downstream of the promoter λP_L into the translation vector
pURV22. This plasmid was derived from p629 (George et al,
1987, Bio/Technology 5:600) from which the coding region for
a portion of the herpes simplex virus type I (HSV-I)
glycoprotein (gD-1) was removed and the ampicillin
10 resistance gene replaced by a kanamycin cassette obtained
from the plasmid vector pUC4K (Pharmacia Biotech Canada
Inc., Baie D'Urfe, Canada). The vector contained a cassette
of the bacteriophage λ cI857 temperature sensitive repressor
gene from which the functional P_R promoter had been deleted.
15 The inactivation of the cI857 repressor by temperature
increase from the ranges of 30-37°C to 37-42°C resulted in
the induction of the gene under the control of λP_L . The
translation of the gene was controlled by the ribosome
binding site cro followed downstream by a BglII restriction
20 site (AGATCT) and the ATG: ACTAAGGAGGTTAGATCTATG.

Restriction enzymes and T4 DNA ligase were used according to
suppliers (Pharmacia Biotech Canada Inc., Baie D'Urfe,
Canada; and New England Biolabs Ltd., Mississauga, Canada).
25 Agarose gel electrophoresis of DNA fragments was performed
as described by Sambrook et al. (Molecular cloning : A
laboratory Manual, 1989, Cold Spring Harbor Laboratory
Press, N.Y). Chromosomal DNA of the GBS bacteria was
prepared according to procedures described in Jayarao et al
30 (J. Clin. Microbiol., 1991, 29:2774). DNA amplification
reactions by polymerase chain reaction (PCR) were made using
DNA Thermal Cycler GeneAmp PCR system 2400 (Perkin Elmer,
San Jose, CA). Plasmids used for DNA sequencing were
purified using plasmid kits from Qiagen (Chatsworth, CA).
35 DNA fragments were purified from agarose gels using Qiaex II

gel extraction kits from Qiagen (Chatsworth, CA). Plasmid transformations were carried out by the method described by Hanahan (DNA Cloning, Glover (ed.) pp, 109-135, 1985). The sequencing of genomic DNA inserts in plasmids was done using
5 synthetic oligonucleotides which were synthesized by oligonucleotide synthesizer model 394 (the Perkin-Elmer Corp., Applied Biosystems Div. (ABI), Foster City, CA). The sequencing reactions were carried out by PCR using the Taq Dye Deoxy Terminator Cycle Sequencing kit (ABI, Foster City,
10 CA) and DNA electrophoresis was performed on automated DNA sequencer 373A (ABI, Foster City, CA). The assembly of the DNA sequence was performed using the program Sequencer 3.0 (Gene Codes Corporation, Ann Arbor, MI). Analysis of the DNA sequences and their predicted polypeptides was performed
15 with the program Gene Works version 2.45 (Intelligenetics, Inc., Mountain View CA).

The coding region of the GBS gene was amplified by PCR from GBS strain C388/90 (Ia/c) genomic DNA using oligos that
20 contained base extensions for the addition of restriction sites BglII (AGATCT) and XbaI (TCTAGA), respectively. The PCR product was purified from agarose gel using a Qiaex II gel extraction kit from Qiagen (Chatsworth, CA), digested with the restriction enzymes BglII and XbaI, and extracted with
25 phenol:chloroform before ethanol precipitation. The pURV22 vector was digested with the restriction enzymes BglII and XbaI, extracted with phenol:chloroform, and ethanol precipitated. The BglII-XbaI genomic DNA fragment was ligated to the BglII-XbaI pURV22 vector in which the GBS
30 gene was under the control of the λ PL promoter. The ligated products were transformed into *E. coli* strain XLI Blue MRF' (Δ (mcrA)183 Δ (mcrCB-hsdSMR-mrr)173 endA1 supE44 thi-1 recA1 gyrA96 relA1 lac[F' proAB lacI^qZAM15 Tn10(Tet^r)]^c) (Stratagene, La Jolla CA) according to the methods described
35 in Hanahan, supra. Transformants harboring plasmids with the

insert were identified by analysis of lysed cells submitted to electrophoresis on agarose gel (Sambrook et al, supra). The recombinant pURV22 plasmid was purified using a Qiagen kit (Qiagen, Chatsworth, CA) and the nucleotide sequence of
5 the DNA insert was verified by DNA sequencing.

The transformant XLI Blue MRF'/rpURV22 was grown at 34°C with agitation at 250 rpm in LB broth containing 50µg of kanamycin per mL until the A₆₀₀ reached a value of 0.6. In
10 order to induce the production of the fusion protein, the cells were incubated for 4 additional hours at 39°C. The bacterial cells were harvested by centrifugation , resuspended in sample buffer, boiled for 10 min and kept at -20°C.

15

EXAMPLE 6 Subcloning GBS protein gene in CMV plasmid pCMV-GH

The DNA coding region of a GBS protein was inserted in phase
20 downstream of the human growth hormone (hGH) gene which was under the transcriptional control of the cytomegalovirus (CMV) promoter in the plasmid vector pCMV-GH (Tang et al, Nature, 1992, 356:152). The CMV promoter is non functional in E. coli cells but active upon administration of the
25 plasmid in eukaryotic cells. The vector also incorporated the ampicillin resistance gene.

The coding region of the gene was amplified by PCR from genomic DNA of GBS strain C388/90 (Ia/c) using the oligos
30 that contained base extensions for the addition of the restriction sites BglII (AGATCT) and HindIII (AAGCTT). The PCR product was purified from agarose gel using a Qiaex II gel extraction kit from Qiagen (Chatsworth, CA), digested with the restriction enzymes BglII and HindIII, and
35 extracted with phenol:chloroform before ethanol precipitation. The pCMV-GH vector (Laboratory of Dr. Stephen

A. Johnston, Department of Biochemistry, The University of Texas, Dallas, Texas) containing the human growth hormone to create fusion proteins was digested with the restriction enzymes BamHI and HindIII, extracted with phenol:chloroform, and ethanol precipitated. The 1.3-kb BglIII-HindIII genomic DNA fragment was ligated to the BamHI -HindIII pCMV-GH vector to create the hGH-GBS fusion protein under the control of the CMV promoter. The ligated products were transformed into *E. coli* strain DH5 α [ϕ 80 *lacZ* Δ M15 *endA*1 *recA*1 *hsdR*17 (^rK^mK⁺) *supE*44 *thi*-1 λ *gyrA*96 *relA*1 Δ (*lacZYA*-*argF*)U169] (Gibco BRL, Gaithersburg, MD) according to the methods described by Hanahan, supra. Transformants harboring plasmids with the insert were identified by analysis of lysed cells submitted to electrophoresis on agarose gel (Sambrook, J. et al, supra). The recombinant pCMV plasmid was purified using a Qiagen kit (Qiagen, Chatsworth, CA) and the nucleotide sequence of the DNA insert was verified by DNA sequencing.

20

EXAMPLE 7 Immunological activity of GBS protein to GBS challenge

Four groups of 12 female CD-1 mice (Charles River, St-Constant, Quebec, Canada) of 6 to 8 weeks were injected subcutaneously three times at three week intervals with 0.1mL of the following antigenic preparations: formaldehyde killed cells of GBS strain C388/90 ($\sim 6 \times 10^7$ cfu), 20 μ g of thioredoxin-His.Tag-GBS fusion protein obtained from the insoluble (inclusion bodies) or 20 μ g of the fusion protein, affinity purified (nickel column), from the soluble cytoplasmic fraction in *E. coli*, or 20 μ g of affinity purified (nickel column) thioredoxin-His.Tag control polypeptide. 20 μ g of QuilATM (Cedarlane Laboratories Ltd, Hornby, Canada)

was added to each antigenic preparation as the adjuvant. Serum samples were obtained from each mouse before immunization (PB) and on days 20 (TB1), 41 (TB2) and 54 (TB3) during the immunization protocols. Sera were frozen
5 at -20°C.

An increase of the ELISA titers was recorded after each injection of the fusion protein indicating a good primary response and a boost of the specific humoral immune response
10 after each of the second and third administration. At the end of the immunization period, the means of reciprocal ELISA titers was 456,145 for the group immunized with 20µg of fusion protein obtained from inclusion bodies compared to 290,133 for the group of mice immunized with the protein
15 from soluble fraction in *E.coli*. The latter result suggests that the protein obtained from inclusion bodies could be more immunogenic than the soluble protein. Analysis of mice sera in ELISA using the affinity purified thioredoxin-His.Tag to coat plates showed that negligible antibody
20 titers are made against the thioredoxin-His.Tag portion of the fusion protein. The reactivity of the sera from mice injected with the recombinant fusion protein was also tested by ELISA against formaldehyde killed whole cells of GBS strain C388/90. The antibodies induced by immunization with
25 recombinant fusion protein also recognized their specific epitopes on GBS cells indicating that their conformation is close enough to the native streptococcal protein to induce cross-reactive antibodies.

30 To verify whether the immune response induced by immunization could protect against GBS infection, mice were challenged with 3.5×10^5 cfu of GBS strains C338/90(Ia/c) and 1.2×10^5 cfu of strain NCS246(II/R) the results of which are illustrated in tables 3 and 4 respectively. Mice immunized
35 with control thioredoxin-His.Tag peptide were not protected against challenge with either GBS strain while those

immunized with formaldehyde killed C388/90 whole cells only provided protection against homologous challenge. The thioredoxin-His.Tag-GBS fusion protein of the invention protected mice from challenge with both GBS strains. Blood
5 and spleen culture of these mice did not reveal the presence of any GBS.

Table 3 Survival from GBS strain C388/90 (Ia/c) challenge¹

immunizing agent	no. mice surviving challenge	% survival
thioredoxin-His.Tag ²	1 / 6	17
formaldehyde killed C388/90 cells ³	6 / 6	100
thioredoxin-His.Tag-GBS fusion (inclusion body preparation) ⁴	6 / 6	100
thioredoxin-His.Tag-GBS fusion (cytoplasmic fraction) ⁴	6 / 6	100

- 5 ¹ intraperitoneal administration with 1 ml Todd-Hewitt culture medium adjusted to 3.5×10^5 cfu;
² 20 μ g administered; posterior legs paralyzed in surviving mouse; GBS detected in blood and spleen;
³ 6×10^7 cfu administered;
⁴ 20 μ g administered.

Table 4 Survival from GBS strain NCS246 (II/R) challenge¹

immunizing agent	no. mice surviving challenge	% survival
thioredoxin-His.Tag ²	0 / 6	0
formaldehyde killed C388/90 cells ³	2 / 6	34
thioredoxin-His.Tag-GBS fusion (inclusion body preparation) ²	5 / 5 ⁴	100
thioredoxin-His.Tag-GBS fusion (cytoplasmic fraction) ²	6 / 6	100

5 ¹ intraperitoneal administration with 1 ml Todd-Hewitt culture medium containing GBS NCS246 (II/R) suspension adjusted to 1.2×10^5 cfu.

² 20µg administered;

³ 6×10^7 cfu administered;

10 ⁴ one mouse died during immunization.

EXAMPLE 8 Immunization with recombinant GBS protein confers protection against experimental GBS infection

15

This example illustrates the protection of mice against fatal GBS infection by immunization with the recombinant protein corresponding to the SEQ ID NO:39.

20 Groups of 10 female CD-1 mice (Charles River) were immunized subcutaneously three times at three-week intervals with 20 µg of recombinant protein purified from E. coli strain BLR (Novagen) harboring the recombinant pURV22 plasmid vector containing the GBS gene corresponding to SEQ ID NO:42 in
 25 presence of 20 µg of QuilA™ adjuvant (Cedarlane Laboratories Ltd, Hornby, Canada) or, as control, with

QuilA™ adjuvant alone in PBS. Blood samples were collected from the orbital sinus on day 1, 22 and 43 prior to each immunization and fourteen days (day 57) following the third injection. One week later the mice were challenged with
5 approximately 10^4 to 10^6 CFU of various virulent GBS strains. Samples of the GBS challenge inoculum were plated on TSA/5% sheep blood agar plates to determine the CFU and to verify the challenge dose. Deaths were recorded for a period of 14 days and on day 14 post-challenge, the surviving mice were
10 sacrificed and blood and spleen were tested for the presence of GBS organisms. The survival data are shown in table 5.

Prechallenge sera were analyzed for the presence of antibodies reactive with GBS by standard immunoassays. Elisa
15 and immunoblot analyses indicated that immunization with recombinant GBS protein produced in *E. coli* elicited antibodies reactive with both, recombinant and native GBS protein. Antibody responses to GBS are described in Example
9.

20

Table 5. Ability of recombinant GBS protein corresponding to SEQ ID NO: 39 to elicit protection against 8 diverse GBS challenge strains

5

Immunogen	Challenge strain		No. alive:	No. dead ¹
	Designation	Type		
rGBS protein none	C388/90	Ia/c	8 : 2 0 : 10	(P<0.0001)
rGBS protein none	NCS 246	II/R	10 : 0 3 : 7	(P=0.0012)
rGBS protein none	ATCC12401	Ib	10 : 0 3 : 7	(P=0.001)
rGBS protein none	NCS 535	V	10 : 0 5 : 5	(P=0.01)
rGBS protein none	NCS 9842	VI	10 : 0 0 : 10	(P<0.0001)
rGBS protein NCS 915-F ³ none	NCS 915	III	7 : 3 1 : 9 4 : 6	(P=0.0007) ²
rGBS protein NCS 954-F none	NCS 954	III/R	7 : 3 4 : 6 1 : 9	(P=0.002)
rGBS protein COH1-F none	COH1	III	4 : 6 3 : 7 0 : 10	(P=0.0004)

¹ Groups of 10 mice per group were used, the number of mice surviving to infection and the number of dead mice are indicated. The survival curves corresponding to recombinant GBS protein-immunized animals were compared to the survival curves corresponding to mock-immunized animals using the log-rank test for nonparametric analysis.

² Comparison analysis to NCS915-F-immunized animals.

³ Animals were immunized with formaldehyde-killed GBS in presence of QuilATM adjuvant.

All hemocultures from surviving mice were negative at day 14 post-challenge. Spleen cultures from surviving mice were negative except for few mice from experiment MB-11.

EXAMPLE 9 Vaccination with the recombinant GBS protein
elicits an immune response to GBS

Groups of 10 female CD-1 mice were immunized subcutaneously
5 with recombinant GBS protein corresponding to SEQ ID NO:39
as described in Example 8. In order to assess the antibody
response to native GBS protein, sera from blood samples
collected prior each immunization and fourteen days after
the third immunization were tested for antibody reactive
10 with GBS cells by ELISA using plates coated with
formaldehyde-killed GBS cells from type III strain NCS 954,
type Ib strain ATCC12401, type V strain NCS 535 or type VI
strain NCS 9842. The specificity of the raised antibodies
for GBS protein was confirmed by Western blot analyses to
15 GBS cell extracts and purified recombinant antigens. The
results shown in Figure 10 clearly demonstrate that animals
respond strongly to recombinant GBS protein used as
immunogens with median reciprocal antibody titers varying
between 12000 and 128000, for sera collected after the third
20 immunization, depending of the coating antigen. All
preimmune sera were negative when tested at a dilution of
1 :100. GBS-reactive antibodies were detectable in the sera
of each animal after a single injection of recombinant GBS
protein.

25

Example 10 Antigenic conservation of the GBS protein of the present invention

Monoclonal antibodies (MAbs) specific to the GBS protein of the present invention were used to demonstrate that this surface antigen is produced by all GBS and that it is also antigenically highly conserved.

A collection of 68 GBS isolates was used to evaluate the reactivity of the GBS-specific MAbs. These strains were obtained from the National Center for Streptococcus, Provincial Laboratory of Public Health for Northern Alberta, Canada; Centre Hospitalier Universitaire de Quebec, Pavillon CHUL, Quebec, Canada; American Type Culture Collection, USA; Laboratoire de Sante Publique du Quebec, Canada; and Dept. of Infectious Disease, Children's Hospital and Medical Center, Seattle, USA. All eight MAbs were tested against the following panel of strains: 6 isolates of serotype Ia or Ia/c, 3 isolates of serotype Ib, 4 isolates of serotype II, 14 isolates of serotype III, 2 isolates of serotype IV, 2 isolates of serotype V, 2 isolates of serotype VI, 2 isolates of serotype VII, 1 isolate of serotype VIII, 10 isolates that were not serotyped and 3 bovine *S. agalactiae* strains. MAb 3A2 was also reacted with additional GBS: 9 isolates of serotype Ia/c and 10 isolates of serotype V. The strains were grown overnight on blood agar plates at 37°C in an atmosphere of 5% CO₂. Cultures were stored at -70°C in heart infusion broth with 20% (v/v) glycerol.

To obtain the GBS protein-specific MAbs, mice were immunized three times at three-week intervals with 20 µg of purified recombinant GBS protein (SEQ ID NO :44) in the presence of 20% QuilA™ adjuvant. Hybridoma cell lines were generated by fusion of spleen cells recovered from immunized mice with the nonsecreting SP2/O myeloma cell line as described

previously (Hamel, J. et al. 1987. J. Med. Microbiol. 23:163-170). Hybrid clone supernatants were tested for specific antibody production by ELISA using formaldehyde inactivated GBS and purified recombinant GBS protein (SEQ ID NO :39 or 44) as coating antigen, as previously described (Hamel, J. et al. 1987. J. Med. Microbiol. 23:163-170). Specific hybrid were cloned by limiting dilutions, expanded, and frozen in liquid nitrogen. Production of recombinant GBS protein was presented in Examples 4 & 5. Purified recombinant GBS protein or formaldehyde inactivated GBS were resolved by electrophoresis by using the discontinuous buffer system of Laemmli as recommended by the manufacturer and then transfer onto nitrocellulose membrane for Western immunoblotting as described previously (Martin et al. 1992. Infect. Immun. 60:2718-2725).

Western immunoblotting experiments clearly indicated that all eight MAbs recognized a protein band that corresponded to the purified recombinant GBS protein (SEQ ID NO :39). These MAbs also reacted with a protein band present in every GBS isolates tested so far. The reactivity of these GBS-specific MAbs are presented in Table 6. Each MAb reacted well with all 46 GBS. In addition, these MAbs also recognized the 3 *S. agalactiae* strains of bovine origin that were tested. MAb 3A2 also recognized nineteen GBS; 9 isolates of serotype Ia/c and 10 of serotype V. The other MAbs were not tested against these additional strains.

These results demonstrated that the GBS protein (SEQ ID NO :39) was produced by all the 65 GBS and the three 3 *S. agalactiae* strains of bovine origin that were tested so far.

More importantly, these results clearly demonstrated that the epitopes recognized by these eight GBS-specific MAbs were widely distributed and conserved among GBS. These results also indicated that these epitopes were not

restricted to serologically related isolates since representatives of all known GBS serotypes including the major disease causing groups were tested.

- 5 In conclusion, the data presented in this example clearly demonstrated that the GBS protein of the present invention is produced by all GBS and that it is antigenically highly conserved.

10

Table 6. Reactivity of eight GBS protein-specific MAb with different *S. agalactiae* strains as evaluated by Western immunoblots.

Mabs	Number of each serotype of <i>s. agalactiae</i> strains recognized by the MAb.										
	Ia or Ia/c (6)	Ib (3)	II (4)	III (4)	IV (2)	V (2)	VI (2)	VII (2)	VIII (1)	NT(10) 2	TOTAL (26)
3A21	6	3	4	4	2	2	2	2	1	10	46
5A12	6	3	4	4	2	2	2	2	1	10	46
6G11	6	3	4	4	2	2	2	2	1	10	46
8B9	6	3	4	4	2	2	2	2	1	10	46
8E11	6	3	4	4	2	2	2	2	1	10	46
12B12	6	3	4	4	2	2	2	2	1	10	46
18F11	6	3	4	4	2	2	2	2	1	10	46
20G2	6	3	4	4	2	2	2	2	1	10	46

1 Nine additional strains of serotype Ia/c and 10 strains of serotype V were recognized by MAb 3A2.

2 These strains were not serotyped

WE CLAIM:

1. An isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide having a sequence selected from the group consisting of:
SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO:10,
SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15,
SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19,
SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24,
SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29,
SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34,
SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39,
SEQ ID NO:40, SEQ ID NO:41 and SEQ ID NO:44 or
fragments, analogs or derivatives thereof.
2. A polynucleotide according to claim 1, wherein said polynucleotide encodes a polypeptide having at least 95% identity to the second polypeptide.
3. An isolated polynucleotide encoding a polypeptide capable of generating antibodies having binding specificity for a polypeptide having a sequence selected from the group consisting of:
SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO:10,
SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15,
SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19,
SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24,
SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29,
SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34,
SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39,
SEQ ID NO:40, SEQ ID NO:41 and SEQ ID NO:44 or
fragments, analogs or derivatives thereof.

4. An isolated polynucleotide that is complementary to the polynucleotide of claim 1.
5. An isolated polynucleotide that is complementary to the polynucleotide of claim 3.
6. The polynucleotide of claim 1, wherein said polynucleotide is DNA.
7. The polynucleotide of claim 3, wherein said polynucleotide is DNA.
8. The polynucleotide of claim 1, wherein said polynucleotide is RNA.
9. The polynucleotide of claim 3, wherein said polynucleotide is RNA.
10. A polynucleotide which hybridizes under stringent conditions to a second polynucleotide having a sequence selected from the group consisting of :
SEQ ID NO : 1, SEQ ID NO : 7, SEQ ID NO : 13, SEQ ID NO : 22, SEQ ID NO : 27, SEQ ID NO : 32, SEQ ID NO : 37, SEQ ID NO : 42 and SEQ ID NO : 43 or fragments, analogues or derivatives thereof.
11. A polynucleotide which hybridizes under stringent conditions to a second polynucleotide having a sequence selected from the group consisting of :
SEQ ID NO : 37, SEQ ID NO : 42 and SEQ ID NO : 43.
12. A polynucleotide according to claim 11 which hybridizes under stringent conditions to a second polynucleotide having the sequence SEQ ID NO : 37.

13. A polynucleotide according to claim 11 which hybridizes under stringent conditions to a second polynucleotide having the sequence SEQ ID NO : 42.
14. A polynucleotide according to claim 11 which hybridizes under stringent conditions to a second polynucleotide having the sequence SEQ ID NO : 43.
15. A polynucleotide according to claim 10 wherein said polynucleotide has at least 95% complementarity to the second polynucleotide.
16. A polynucleotide according to claim 11 wherein said polynucleotide has at least 95% complementarity to the second polynucleotide.
17. A vector comprising the polynucleotide of claim 1, wherein said polynucleotide is operably linked to an expression control region.
18. A vector comprising the polynucleotide of claim 3, wherein said polynucleotide is operably linked to an expression control region.
19. A host cell transfected with the vector of claim 17.
20. A host cell transfected with the vector of claim 18.
21. A process for producing a polypeptide comprising culturing a host cell according to claim 19 under conditions suitable for expression of said polypeptide.
22. A process for producing a polypeptide comprising culturing a host cell according to claim 20 under condition suitable for expression of said polypeptide.

23. An isolated polypeptide having at least 70% identity to a second polypeptide having a sequence selected from the group consisting of:
SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO:10,
SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15,
SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19,
SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24,
SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29,
SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34,
SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39,
SEQ ID NO:40, SEQ ID NO:41 and SEQ ID NO:44 or
fragments, analogs or derivatives thereof.
24. The isolated polypeptide of claim 23 having a sequence according to SEQ ID NO : 39.
25. The isolated polypeptide of claim 23 having a sequence according to SEQ ID NO : 44.
26. An isolated polypeptide capable of generating antibodies having binding specificity for a second polypeptide having a sequence selected from the group consisting of:
SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO:10,
SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15,
SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19,
SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24,
SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29,
SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34,
SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39,
SEQ ID NO:40, SEQ ID NO:41 and SEQ ID NO:44 or
fragments, analogs or derivatives thereof.

27. The isolated polypeptide of claim 26 having a sequence according to SEQ ID NO : 39.
28. The isolated polypeptide of claim 26 having a sequence according to SEQ ID NO : 44.
29. An isolated polypeptide having an amino acid sequence selected from the group consisting of:
SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO:10,
SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15,
SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19,
SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24,
SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29,
SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34,
SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39,
SEQ ID NO:40 and SEQ ID NO:41 or fragments, analogs or derivatives thereof.
30. The isolated polypeptide of claim 29 having an amino acid sequence according to SEQ ID NO : 39.
31. An isolated polypeptide having an amino acid sequence according to SEQ ID NO : 44.
32. An isolated polypeptide according to any one of claims 29 to 31, wherein the N-terminal Met residue is deleted.
33. An isolated polypeptide according to any one of claims 29 to 30, wherein the secretory amino acid sequence is deleted.
34. A vaccine composition comprising a polypeptide according to any one of claims 23 to 31 and a pharmaceutically acceptable carrier, diluent or adjuvant.

35. A vaccine composition comprising a polypeptide according to claim 32 and a pharmaceutically acceptable carrier, diluent or adjuvant.
36. A vaccine composition comprising a polypeptide according to claim 33 and a pharmaceutically acceptable carrier, diluent or adjuvant.
37. A method for therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of a composition according to claim 34.
38. A method for therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of a composition according to claim 35.
39. A method for therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of a composition according to claim 36.
40. A method according to any one of claims 37 to 39, wherein said animal is a bovine.
41. A method according to any one of claims 37 to 39, wherein said animal is a human.

42. A method according to any one of claims 37 to 39, wherein said bacterial infection is selected from the group consisting of group A streptococcus and group B streptococcus.
43. A method according to claim 42, wherein said bacterial infection is group B streptococcus.
44. Use of a vaccine composition according to claim 34 for the therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to or infected with streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of the composition.
45. Use of a vaccine composition according to any one of claims 35 to 36 for the therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to or infected with streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of the composition.
46. Use of a vaccine composition according to any one claims 23 to 31 for the manufacture of a vaccine for the therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of the composition.
47. Use of a vaccine composition according to claim 32 for the manufacture of a vaccine for the therapeutic or

prophylactic treatment of streptococcal bacterial infection in an animal susceptible to streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of the composition.

48. Use of a vaccine composition according to claim 33 for the manufacture of a vaccine for the therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of the composition.

TATCTGGCAA AGAGCCAGCT AATCGTTTTA GTTGGGCTAA AAATAAATTA TTAATCAATG 60
S G K E P A N R F S W A K N K L L I N G
---->
GATTCATTGC AACTCTAGCA GCAACTATCT TATTTTTTGC AGTTCAATTC ATAGGTCTTA 120
F I A T L A A T I L F F A V Q F I G L K
AACCAGATTA CCCTGGAAAA ACCTACTTTA TTATCCTATT GACAGCATGG ACTTTGATGG 180
P D Y P G K T Y F I I L L T A W T L M A
CATTAAGTAAC TGCTTTAGTG GGATGGGATA ATAGGTATGG TTCCTTCTTG TCGTTATTAA 240
L V T A L V G W D N R Y G S F L S L L I
TATTATTATT CCAGCTTGGT TCAAGCGCAG GAACTTACCC AATAGAATTG AGTCCTAAGT 300
L L F Q L G S S A G T Y P I E L S P K F
TCTTTCAAAC AATTCAACCA TTTTACC GA TACTTACTC TGTTCAGGA TTAAGAGAGA 360
F Q T I Q P F L P M T Y S V S G L R E T
CCATCTCGTT GACGGGAGAC GTTAACCATC AATGGAGAAT GCTAGTAATC TTTTATAGTAT 420
I S L T G D V N H Q W R M L V I F L V S
CATCGATGAT ACTTGCTCTT CTTATTTATC GTAAACAAGA AGATTAATAG AAAGTATCTA 480
S M I L A L L I Y R K Q E D
GTGATAGACT AACAGTATGA TATGGTATGT CAAAGTATTT AGGAGGAGAA GATATGTCTA 540
M S T
|---->
CTTTAACAAT AATTATTGCA ACATTAAGT CTTTGGACA TTTTATATT ATGTATTTGG 600
L T I I I A T L T A L E H F Y I M Y L E
AGACGTTAGC CACCCAGTCA AATATGACTG GGAAGATTTT TAGTATGTCT AAAGAAGAGT 660
T L A T Q S N M T G K I F S M S K E E L
TGTCATATTT ACCCGTTATT AAACCTTTTA AGAATCAAGG TGTATACAAC GGCTTGATTG 720
S Y L P V I K L F K N Q G V Y N G L I G
GCCTATTCCT CCTTTATGGG TTATATATTT CACAGAATCA AGAAATTGTA GCTGTTTTTT 780
L F L L Y G L Y I S Q N Q E I V A V F L
TAATCAATGT ATTGCTAGTT GCTATTTATG GTGCTTTGAC AGTTGATAAA AAAATCTTAT 840
I N V L L V A I Y G A L T V D K K I L L
TAAACAGGG TGGTTTACCT ATATTAGCTC TTTTAACATT CTTATTTTAA TACTACTTAG 900
K Q G G L P I L A L L T F L F
CCGTTCGATT TAGTTGAACG GCTTTTAGTA ATCATTTTTT TCTCATAATA CAGGTAGTTT 960
AAGTAATTTG TCTTTAAAA TAGTATAATA TAACTACGAA TTCAAAGAGA GGTGACTTTG 1020
ATTATGACTG AGAACTGGTT ACATACTAAA GATGGTTCAG ATATTTATTA TCGTGTCGTT 1080
M T E N W L H T K D G S D I Y Y R V V
|---->
GGTCAAGGTC AACCGATTGT TTTTACAT GGCAATAGCT TAAGTAGTCG CTATTTTGAT 1140
G Q G Q P I V F L H G N S L S S R Y F D
AAGCAAATAG CATATTTTTC TAAGTATTAC CAAGTTATTG TTATGGATAG TAGAGGGCAT 1200
K Q I A Y F S K Y Y Q V I V M D S R G H
GGCAAAAGTC ATGCAAAGCT AAATACCATT AGTTTCAGGC AAATAGCAGT TGAAGTAAAG 1260
G K S H A K L N T I S F R Q I A V D L K

GATATCTTAG TTCATTTAGA GATTGATAAA GTTATATTGG TAGGCCATAG CGATGGTGCC 1320
D I L V H L E I D K V I L V G H S D G A

AATTTAGCTT TAGTTTTTCA AACGATGTTT CCAGGTATGG TTAGAGGGCT TTTGCTTAAT 1380
N L A L V F Q T M F P G M V R G L L L N

TCAGGGAACC TGACTATTCA TGGTCAGCGA TGGTGGGATA TTCTTTTAGT AAGGATTGCC 1440
S G N L T I H G Q R W W D I L L V R I A

TATAAATTCC TTCACTATTT AGGGAAACTC TTTCCGTATA TGAGGC AAAA AGCTCAAGTT 1500
Y K F L H Y L G K L F P Y M R Q K A Q V

ATTTGCTTA TGTGGAGGA TTTGAAGATT AGTCCAGCTG ATTTACAGCA TGTGTCAACT 1560
I S L M L E D L K I S P A D L Q H V S T

CCTGTAATGG TTTTGGTTGG AAATAAGGAC ATAATTAAGT TAAATCATTC TAAGAACTT 1620
P V M V L V G N K D I I K L N H S K K L

GCTTCTTATT TTCCAAGGGG GGAGTTTTAT TCTTTAGTTG GCTTTGGGCA TCACATTATT 1680
A S Y F P R G E F Y S L V G F G H H I I

AAGCAAGATT CCCATGTTTT TAATATTATT GCAAAAAAGT TTATCAACGA TACGTTGAAA 1740
K Q D S H V F N I I A K K F I N D T L K

GGAGAAATTG TTGAAAAAGC TAATTGAAAA AGTCAAATCA CTGACTTCTG TGATTAAAAT 1800
G E I V E K A N

TGTATTTTTT ATATCTGTTT TAGTGCTTAT TATTGTTGAA ATGATTCATT TGAAACGAAC 1860
M I H L K R T
|---->

TATTTCTGTT GAGCAACTAA AGAGTGTTTT TGGGCAATTA TCTCCAATGA ATCTTTTCTT 1920
I S V E Q L K S V F G Q L S P M N L F L

AATTATCCTT GTGGGGGTTA TCGCTGTCTT ACCGACAACC GGATATGACT TTGTACTGAA 1980
I I L V G V I A V L P T T G Y D F V L N

TGGACTTTTA CGTACAGATA AAAGCAAAAG GTATATTTTA CAGACTAGTT GGTGTATCAA 2040
G L L R T D K S K R Y I L Q T S W C I N

CACTTTTAAT AACTTGTCAG GATTCGGTGG CTTAATCGAT ATTGGGTTGC GCATGGCTTT 2100
T F N N L S G F G G L I D I G L R M A F

TTATGGTAAA AAAGGTCAAG AGAAGAGTGA CCTAAGAGAA GTGACTCGTT TTTTACCCTA 2160
Y G K K G Q E K S D L R E V T R F L P Y

TCTTATTCTT GGTCTGTCAT TTATTAGTGT GATTGCCTTA ATCATGAGCC ATATTTTCTA 2220
L I S G L S F I S V I A L I M S H I F H

TGCCAAAGCT AGTGTTGATT ACTATTATTT GGTATTAATT GGTGCTAGTA TGTATTTTCC 2280
A K A S V D Y Y Y L V L I G A S M Y F P

TGTTATTTAT TGGATTTCTG GTCATAAAGG AAGCCATTAT TTCGGAGATA TGCCATCTAG 2340
V I Y W I S G H K G S H Y F G D M P S S

TACTCGTATA AAATTAGGTG TTGTTTCTTT TTTTGAATGG GGATGTGCGG CCGCAGCATT 2400
T R I K L G V V S F F E W G C A A A A F

TATAATTATC GGTTATTTAA TGGGCATTCA TCTACCAGTT TATAAAATTT TACCACTATT 2460
I I I G Y L M G I H L P V Y K I L P L F

TTGTATTGGT TGTGCCGTCG GGATTGTATC CCTTATTCCT GGTGGATTAG GAAGTTTGA 2520
C I G C A V G I V S L I P G G L G S F E

ATTAGTTCTA TTTACAGGGT TTGCTGCCGA GGGACTACCT AAAGAACTG TGGTTGCATG 2580
L V L F T G F A A E G L P K E T V V A W

GTTATTACTT TATCGTTTAG CCTACTATAT TATTCCATTTC TTTGCAGGTA TCTATTTCTT 2640
L L L Y R L A Y Y I I P F F A G I Y F F

TATCCATTAT TTAGGTAGTC AAATAAATCA ACGTTATGAA AATGTCCCGA AAGAGTTAGT 2700
I H Y L G S Q I N Q R Y E N V P K E L V

ATCAACTGTT CTACAAACCA TGGTGAGCCA TTTGATGCGT ATTTTAGGTG CATTCTTAAT 2760
S T V L Q T M V S H L M R I L G A F L I
|---->

ATTTTCAACA GCATTTTTTG AAAATATTAC TTATATTATG TGGTTGCAGA AGCTAGGCTT 2820
F S T A F F E N I T Y I M W L Q K L G L

GGACCCATTA CAAGAACAAA TGTTATGGCA GTTTCAGGT TTATTGCTGG GGGTTTGT 2880
D P L Q E Q M L W Q F P G L L L G V C F

TATTCTCTTA GCTAGAACTA TTGATCAAAA AGTGAAAAAT GCTTTTCCAA TTGCTATTAT 2940
I L L A R T I D Q K V K N A F P I A I I

CTGGATTACT TTGACATTGT TTTATCTTAA TTTAGGTCAT ATTAGTTGGC GACTATCTTT 3000
W I T L T L F Y L N L G H I S W R L S F

CTGGTTTATT TTACTATTGT TAGGCTTATT AGTCATTAAG CCAACTCTCT ATAAAAACA 3060
W F I L L L L G L L V I K P T L Y K K Q

ATTATTTAT AGCTGGGAAG AGCGTATTAA GGATGGAATC ATTATCGTTA GTTTAATGGG 3120
F I Y S W E E R I K D G I I I V S L M G

AGTTCTATTT TATATTGCAG GACTACTATT CCCTATCAGG GCTCATATTA CAGGTGGTAG 3180
V L F Y I A G L L F P I R A H I T G G S

TATTGAACGC CTGCATTATA TCATAGCATG GGAGCCGATA GCATTGGCTA CGTTGATTCT 3240
I E R L H Y I I A W E P I A L A T L I L

TACTCTCGTT TATTTATGTT TGGTTAAGAT TTTACAAGGA AAATCTTGTC AGATTGGTGA 3300
T L V Y L C L V K I L Q G K S C Q I G D

TGTGTTCAAT GTGGATCGTT ATAAAAAACT ACTTCAAGCT TACGGTGGTT CTTCGGATAG 3360
V F N V D R Y K K L L Q A Y G G S S D S

CGGTTTAGCC TTTTAAATG ATAAAAGGCT CTACTGGTAC CAAAAAATG GAGAAGATTG 3420
G L A F L N D K R L Y W Y Q K N G E D C

CGTTGCGTTC CAATTTGTAA TTGTCAATAA TAAATGTCTT ATTATGGGGG AACCAGCCGG 3480
V A F Q F V I V N N K C L I M G E P A G

TGATGACACT TATATTCGTG AAGCTATTGA ATCGTTTATT GATGATGCTG ATAAGCTAGA 3540
D D T Y I R E A I E S F I D D A D K L D

CTATGACCTT GTTTTTTACA GTATTGGACA GAAGTTGACA CTACTTTTAC ATGAGTATGG 3600
Y D L V F Y S I G Q K L T L L L H E Y G

TTTTGACTTT ATGAAAGTTG GTGAGGATGC TTTAGTTAAT TTAGAAACGT TTACTCTTAA 3660
F D F M K V G E D A L V N L E T F T L K

AGGGAATAAG TACAAACCTT TCAGAAATGC CCTAAATAGA GTTGAAAAGG ATGGTTTCTA	3720
G N K Y K P F R N A L N R V E K D G F Y	
TTTCGAAGTT GTACAATCGC CACATAGTCA AGAGCTACTA AATAGTTTGG AAGAGATTTC	3780
F E V V Q S P H S Q E L L N S L E E I S	
TAATACTTGG TTAGAAGGAC GTCCTGAAAA AGGTTTCTCA CTAGGATATT TTAATAAAGA	3840
N T W L E G R P E K G F S L G Y F N K D	
TTATTTCCAA CAAGCCCCAA TAGCTTTGGT AAAAAATGCT GAACACGAAG TTGTTGCTTT	3900
Y F Q Q A P I A L V K N A E H E V V A F	
TGCTAATATT ATGCCAAACT ATGAAAAGAG TATTATCTCT ATTGATTAA TCGGTCACGA	3960
A N I M P N Y E K S I I S I D L M R H D	
TAAACAGAAA ATTCCGAATG GCGTTATGGA TTTCCTCTTT TTATCATTAT TCTCTTATTA	4020
K Q K I P N G V M D F L F L S L F S Y Y	
TCAAGAGAAG GGATACCACT ATTTTGATTT GGGGATGGCA CCTTTATCAG GAGTTGGTCG	4080
Q E K G Y H Y F D L G M A P L S G V G R	
CGTTGAAACA AGTTTGTCTA AAGAGAGAAT GGCGTATCTT GTCTATCATT TCGGTAGTCA	4140
V E T S F A K E R M A Y L V Y H F G S H	
TTTCTACTCA TTTAATGGTT TACACAAGTA TAAGAAGAAG TTTACACCAT TGTGGTCGGA	4200
F Y S F N G L H K Y K K K F T P L W S E	
ACGTTATATT TCTTGTTCTC GTTCGTCCTG GTTAATTTGT GCTATTTGTG CCCTATTAAT	4260
R Y I S C S R S S W L I C A I C A L L M	
GGAAGATAGT AAAATTAAGA TTGTAAATA AGCTTTATTT GGCAATTAAA AAGAGCATGT	4320
E D S K I K I V K	
CATGCGACAT GCTCTTTTAA AATCATTTAA TACCATTGAT TGCTTGAATC TACTTTATAA	4380
TATGATGTGC TTTTAAATAT TGTTTAGCTA CTGTAGCTGC TGATTTATGC TTTACAGCTA	4440
CTTGGTAGTT CATTTCTTGC ATTTCTTTTT CAGTGATATG ACCAGCAAGT TTATTGAGAG	4500
CTTTTTTTAC TTGA (SEQ ID NO:1)	4514

FIG. 1a
[clone1-dna/aa]

SGKEPANRFS WAKNKLLING FIATLAATIL FFAVQFIGLK PDYPGKTYFI 50
ILLTAWTLMA LVTALVGWDN RYGSFLSLLI LLFQLGSSAG TYPIELSPKF 100
FQTIQPFLPM TYSVSGLRET ISLTGDVNHQ WRMLVIFLVS SMILALLIYR 150
KQED (SEQ ID NO:2) 154

FIG. 1b

MSTLTIIAT LTALEHFYIM YLETLATQSN MTGKIFSMSK EELSYLPVIK 50
LFKNQGVYNG LIGLFLLYGL YISQNQEIVA VFLINVLLVA IYGALTVDKK 100
ILLKQGGLPI LALLTFLF (SEQ ID NO:3) 118

FIG. 1c

MTENWLHTKD GSDIYYRVVG QGQPIVFLHG NSLSSRYFDK QIAYFSKYYQ 50
VIVMDSRGHG KSHAKLNTIS FRQIAVDLKD ILVHLEIDKV ILVGHS DGAN 100
LALVFQTMFP GMVRGLLLNS GNLTIHGQRW WDILLVRIAY KFLHYLGKLF 150
PYMRQKAQVI SLMLLEDLKIS PADLQHVSTP VMVLVGNKDI IKLNHKKLA 200
SYFPRGEFYS LVGFGHHIHK QDSHVFNIIA KKFINDTLKG EIVEKAN 247
(SEQ ID NO:4)

FIG. 1d

MIHLKRTISV	EQLKSVFGQL	SPMNLFLIIL	VGVI AVLPTT	GYDFVLNGLL	50
RTDKSKRYIL	QTSWCINTFN	NLSGFGGLID	IGLRMAFYGK	KGQEKSDLRE	100
VTRFLPYLIS	GLSFISVIAL	IMSHIFHAKA	SVDYYYLVLI	GASMYFPVIY	150
WISGHKGSHY	FGDMPSSTRI	KLGVSFFFEW	GCAAAAFIII	GYLMGIHLPV	200
YKILPLFCIG	CAVGIVSLIP	GGLGSFELVL	FTGFAAEGLP	KETVVAWLLL	250
YRLAYYIIPF	FAGIYFFIHY	LGSQINQRYE	NVPKELVSTV	LQTMVSHLMR	300
ILGAFLIFST	AFFENITYIM	WLQKLGLDPL	QEOMLWQFPG	LLLGVCFILL	350
ARTIDQKVKN	AFPIAIIWIT	LTLFYLN LGH	ISWRLSEFWI	LLLLGLLVIK	400
PTLYKKQFIY	SWEERIKDGI	IIVSLMGVLF	YIAGLLFPIR	AHITGGSIER	450
LHYIIAWEPI	ALATLILTLV	YLCLVKILQG	KSCQIGDVFN	VDRYKKLLQA	500
YGGSSDSGLA	FLNDKRLYWY	QKNGEDCVAF	QFVIVNNKCL	IMGEPAGDDT	550
YIREAIESFI	DDADKLDYDL	VFYSIGQKLT	LLLHEYGFDF	MKVGEDALVN	600
LETFTLKG NK	YKPFERNALNR	VEKDG FYFEV	VQSPHSQELL	NSLEEISNTW	650
LEGRPEKGFS	LGYFNKD YFQ	QAPIALVKNA	EHEVVAFANI	MPNYEKSIIS	700
IDLMRHDKQK	IPNGVMDFLF	LSLFSYYQEK	GYHYFDLGMA	PLSGVGRVET	750
SFAKERMAYL	VYHFGSHFYS	FNGLHKYKKK	FTPLWSERYI	SCSRSSWLIC	800
AICALLMEDS	KIKIVK	(SEQ ID NO:5)			816

FIG. 1e

MRILGAFLIF	STAFFENITY	IMWLQKLGLD	PLQEOMLWQF	PGLLLGVCFI	50
LLARTIDQKV	KNAFPIAIIW	ITLTLFYLN L	GHISWRLSEF	FILLLLGLLV	100
IKPTLYKKQF	IYSWEERIKD	GIIIVSLMGV	LFYIAGLLFP	IRAHITGGSI	150
ERLHYIIAWE	PIALATLILT	LVYLCLVKIL	QKSCQIGDV	FNVD RYKKLL	200
QAYGGSSDSG	LAFLNDKRLY	WYQKNGEDCV	AFQFVIVNNK	CLIMGEPAGD	250
DTYIREAIES	FIDDADKLDY	DLVFYSIGQK	LTL LLHEYGF	DFMKVGEDAL	300
VNLETFTLKG	NKYKPFERNAL	NRVEKDG FYF	EVVQSPHSQE	LLNSLEEISN	350
TWLEGRPEKG	FSLGYFNKDY	FQQAPIALVK	NAEHEVVAFA	NIMP NYEKSI	400
ISIDLMRHDK	QKIPNGVMDF	LFLSLFSYYQ	EKG YHYFDLG	MAPLSGVGRV	450
ETSFAKERMA	YLVYHFGSHF	YSFNGLHKYK	KKFTPLWSER	YISCSRSSL	500
ICAICALLME	DSKIKIVK	(SEQ ID NO:6)			518

FIG. 1f

AATTTTGATA TCGAAACAAC AACTTTTGAG GCAATGAAAA AGCACGCGTC ATTATTGGAG 60
 N F D I E T T T F E A M K K H A S L L E
 ---->
 AAAATATCTG TTGAGCGTTC TTTTATTGAA TTTGATAAAC TTCTATTAGC ACCTTATTGG 120
 K I S V E R S F I E F D K L L L A P Y W
 CGTAAAGGAA TGCTGGCACT AATAGATAGT CATGCTTTTA ATTATCTACC ATGCTTAAAA 180
 R K G M L A L I D S H A F N Y L P C L K
 AATAGGGAAT TACAATTAAG CGCCTTTTGT TCCCAGTTAG ATAAAGATTT TTTATTTGAG 240
 N R E L Q L S A F L S Q L D K D F L F E
 ACATCAGAAC AAGCTTGGGC ATCACTCATC TTGAGTATGG AAGTTGAACA CACAAAGACT 300
 T S E Q A W A S L I L S M E V E H T K T
 TTTTAAAAA AATGGAAGAC ATCAACTCAC TTTCAAAAAG ATGTTGAGCA TATAGTGGAT 360
 F L K K W K T S T H F Q K D V E H I V D
 GTTTATCGTA TTCGTGAACA AATGGGATTG GCTAAAGAAC ATCTTTATCG TTATGGAAAA 420
 V Y R I R E Q M G L A K E H L Y R Y G K
 ACTATAATAA AACAAAGCGGA AGGTATTCGC AAAGCAAGAG GCTTGATGGT TGATTTGAA 480
 T I I K Q A E G I R K A R G L M V D F E
 AAAATAGAAC AACTAGATAG TGAGTTAGCA ATCCATGATA GGCATGAGAT AGTTGTCAAT 540
 K I E Q L D S E L A I H D R H E I V V N
 GGTGGCACCT TAATCAAGAA ATTAGGAATA AAACCTGGTC CACAGATGGG AGATATTATC 600
 G G T L I K K L G I K P G P Q M G D I I
 TCTCAAATTG AATTAGCCAT TGTTTTAGGA CAACTGATTA ATGAAGAAGA GGCTATTTTA 660
 S Q I E L A I V L G Q L I N E E E A I L
 CATTTTGTTA AGCAGTACTT GATGGATTAG AGAGGATTAT ATGAGCGATT TTTTAGTAGA 720
 H F V K Q Y L M D M S D F L V D
 |----->
 TGGATTGACT AAGTCGGTTG GTGATAAGAC GGTCTTTAGT AATGTTTCAT TTATCATCCA 780
 G L T K S V G D K T V F S N V S F I I H
 TAGTTTAGAC CGTATTGGGA TTATTGGTGT CAATGGAAC TGGAAAGACAA CACTATTAGA 840
 S L D R I G I I G V N G T G K T T L L D
 TGTTATTTTCG GGTGAATTAG GTTTTGATGG TGATCGTTCC CCTTTTTCAT CAGCTAATGA 900
 V I S G E L G F D G D R S P F S S A N D
 TTATAAGATT GCTTATTTAA AACAAGAACC AGACTTTGAT GATTCTCAGA CAATTTTGGA 960
 Y K I A Y L K Q E P D F D D S Q T I L D
 CACCGTACTT TCTTCTGACT TAAGAGAGAT GGCTTTAATT AAAGAATATG AATTATTGCT 1020
 T V L S S D L R E M A L I K E Y E L L L
 TAATCACTAC GAAGAAAGTA AGCAATCACG TCTAGAGAAA GTAATGGCAG AAATGGATTG 1080
 N H Y E E S K Q S R L E K V M A E M D S
 TTTAGATGCT TGGTCTATTG AGAGCGAAGT CAAAACAGTA TTATCCAAAT TAGGTATTAC 1140
 L D A W S I E S E V K T V L S K L G I T
 TGATTTGCAG TTGTCGGTTG GTGAATTATC AGGAGGATTA CGAAGACGTG TTCAATTAGC 1200
 D L Q L S V G E L S G G L R R R V Q L A

GCAAGTATTA	TTAAATGATG	CAGATTTATT	GCTCTTAGAC	GAACCTACTA	ACCACTTAGA	1260
Q V L	L N D A	D L L	L L D	E P T N	H L D	
TATTGACACT	ATTGCATGGT	TAACGAATTT	TTTGAAAAAT	AGTAAAAAGA	CAGTGCTTTT	1320
I D T	I A W L	T N F	L K N	S K K T	V L F	
TATAACTCAT	GATCGTTATT	TTCTAGACAA	TGTTGCAACA	CGTATTTTGT	AATTAGATAA	1380
I T H	D R Y F	L D N	V A T	R I F E	L D K	
GGCACAGATT	ACAGAATATC	AAGGCAATTA	TCAGGATTAT	GTCCGACTTC	GTGCAGAACA	1440
A Q I	T E Y Q	G N Y	Q D Y	V R L R	A E Q	
AGACGAGCGT	GATGCTGCTA	GTTTACATAA	AAAGAAACAG	CTTTATAAAC	AGGAACTAGC	1500
D E R	D A A S	L H K	K K Q	L Y K Q	E L A	
TTGGATGCGT	ACTCAGCCAC	AAGCTCGTGC	AACGAAACAA	CAGGCTCGTA	TTAATCGTTT	1560
W M R	T Q P Q	A R A	T K Q	Q A R I	N R F	
TCAAAATCTA	AAAAACGATT	TACACCAAAC	AAGCGATACA	AGCGATTGTG	AAATGACATT	1620
Q N L	K N D L	H Q T	S D T	S D L E	M T F	
TGAAACAAGT	CGAATTGGGA	AAAAGGTTAT	TAATTTTGAA	AATGTCTCTT	TTTCTTACCC	1680
E T S	R I G K	K V I	N F E	N V S F	S Y P	
AGATAAATCT	ATCTTGAAAG	ACTTTAATTT	GTTAATTCAA	AATAAAGACC	GTATTGGCAT	1740
D K S	I L K D	F N L	L I Q	N K D R	I G I	
CGTTGGAGAT	AATGGTGTTG	GAAAGTCAAC	CTTACTTAAT	TTAATTGTTC	AAGATTTACA	1800
V G D	N G V G	K S T	L L N	L I V Q	D L Q	
GCCGGATTCTG	GGTAATGTCT	CTATTGGTGA	AACGATACGT	GTAGGTTACT	TTTCACAACA	1860
P D S	G N V S	I G E	T I R	V G Y F	S Q Q	
ACTTCATAAT	ATGGATGGCT	CAAAACGTGT	TATTAATTAT	TTGCAAGAGG	TTGCAGATGA	1920
L H N	M D G S	K R V	I N Y	L Q E V	A D E	
GGTTAAAACT	AGTGTCGGTA	CAACAAGTGT	GACAGAACTA	TTGGAACAAT	TTCTCTTTCC	1980
V K T	S V G T	T S V	T E L	L E Q F	L F P	
ACGTTGACAC	CATGGAACAC	AAATTGCAAA	ATTATCAGGT	GGTGAGAAAA	AAAGACTTTA	2040
R S T	H G T Q	I A K	L S G	G E K K	R L Y	
CCTTTTAAAA	ATCCTGATTG	AAAAGCCTAA	TGTGTTACTA	CTTGATGAGC	CGACAAATGA	2100
L L K	I L I E	K P N	V L L	L D E P	T N D	
CTTAGATATT	GCTACATTAA	CTGTTCTTGA	AAATTTTSTA	CAAGGCTTTG	GTGGTCCTGT	2160
L D I	A T L T	V L E	N F L	Q G F G	G P V	
GATTACAGTT	AGTCACGATC	GTTACTTTTT	AGATAAAGTG	GCTAATAAAA	TTATTGCGTT	2220
I T V	S H D R	Y F L	D K V	A N K I	I A F	
TGAAGATAAC	GATATCCGTG	AATTTTTTGG	TAATTATACT	GATTATTTAG	ATGAAAAAGC	2280
E D N	D I R E	F F G	N Y T	D Y L D	E K A	
ATTTAATGAG	CAAAATAATG	AAGTTATCAG	TAAAAAAGAG	AGTACCAAGA	CAAGTCGTGA	2340
F N E	Q N N E	V I S	K K E	S T K T	S R E	
AAAGCAAAGT	CGTAAAAGAA	TGTCTTACTT	TGAAAAACAA	GAATGGGCGA	CAATTGAAGA	2400
K Q S	R K R M	S Y F	E K Q	E W A T	I E D	
CGATATTATG	ATATTGGAAA	ATACTATCAC	TCGTATAGAA	AATGATATGC	AAACATGTGG	2460

D I M I L E N T I T R I E N D M Q T C G
 TAGTGATTTT ACAAGGTTAT CTGATTTACA AAAGGAATTA GATGCAAAAA ATGAAGCACT 2520
 S D F T R L S D L Q K E L D A K N E A L
 TCTAGAAAAG TATGACCGTT ATGAGTACCT TAGTGAGTTA GACACATGAT TATCCGTCCG 2580
 L E K Y D R Y E Y L S E L D T M I I R P
 |----->
 ATTATTAAAA ATGATGACCA AGCAGTTGCA CAATTAATTC GACAAAGTTT ACGCGCCTAT 2640
 I I K N D D Q A V A Q L I R Q S L R A Y
 GATTTAGATA AACCTGATAC AGCATATTCA GACCCTCACT TAGATCATTG GACCTCATAC 2700
 D L D K P D T A Y S D P H L D H L T S Y
 TACGAAAAAA TAGAGAAGTC AGGATTCTTT GTCATTGAGG AGAGAGATGA GATTATTGGC 2760
 Y E K I E K S G F F V I E E R D E I I G
 TGTGGCGGCT TTGGTCCGCT GAAAAATCTA ATTGCAGAGA TGCAGAAGGT GTACATTGCA 2820
 C G G F G P L K N L I A E M Q K V Y I A
 GAACGTTTCC GTGGTAAGGG GCTTGCTACT GATTTAGTGA AAATGATTGA AGTAGAAGCT 2880
 E R F R G K G L A T D L V K M I E V E A
 CGAAAAATTG GGTATAGACA ACTTTATTTA GAGACAGCCA GTACTTTGAG TAGGGCAACT 2940
 R K I G Y R Q L Y L E T A S T L S R A T
 GCGGTTTATA AGCATATGGG ATATTGTGCC TTATCGCAAC CAATAGCAAA TGATCAAGGT 3000
 A V Y K H M G Y C A L S Q P I A N D Q G
 CATAAGCTA TGGATATTTG GATGATTAAA GATTTATAAG TTGAAAGTGG ATTAGTGAAC 3060
 H T A M D I W M I K D L
 ATGGATTAAT TATTTTGAGA TAAGAGGAAA GAAAAGGAGA CATATATGGC ATATATTTGG 3120
 M A Y I W
 |----->
 TCTTATTTGA AAAGGTACCC CAATTGGTTA TGGCTTGATT TACTAGGAGC TATGCTTTTT 3180
 S Y L K R Y P N W L W L D L L G A M L F
 GTGACGGTTA TCCTAGGAAT GCCACAGCC TTAGCGGGTA TGATTGATAA TGGCGTTACA 3240
 V T V I L G M P T A L A G M I D N G V T
 AAAGGTGATC GGAAGTGGAGT TTATCTGTGG ACGTTCATCA TGTTTATATT TGTTGTACTA 3300
 K G D R T G V Y L W T F I M F I F V V L
 GGTATTATTG GGCCTATTAC GATGGCTTAC GCATCTAGTC GCTTAACGAC AACAATGATT 3360
 G I I G R I T M A Y A S S R L T T T M I
 AGAGATATGC GTAATGATAT GTATGCTAAG CTTCAAGAAT ACTCCCATCA TGAATATGAA 3420
 R D M R N D M Y A K L Q E Y S H H E Y E
 CAGATAGGTG TATCTTCACT AGTGACACGT ATGACAAGCG ATACTTTTGT TTTGATGCAA 3480
 Q I G V S S L V T R M T S D T F V L M Q
 TTTGCTGAAA TGTCTTTACG TTTAGGCCTA GTAACCTCCTA TGGTAATGAT TTTTAGCGTG 3540
 F A E M S L R L G L V T P M V M I F S V
 GTTATGATAC TAATTACGAG TCCATCTTTG GCTTGGCTTG TAGCGGTTGC GATGCCTCTT 3600
 V M I L I T S P S L A W L V A V A M P L
 TTGGTAGGAG TCGTTTTATA TGTAAGCTATA AAAACAAAAC CTTTATCTGA AAGACAACAG 3660
 L V G V V L Y V A I K T K P L S E R Q Q

ACTATGCTTG ATAAAATCAA TCAATATGTT CGTGAAAATT TAACAGGGTT ACGCGTTGTT 3720
T M L D K I N Q Y V R E N L T G L R V V

AGAGCCTTTG CAAGAGAGAA TTTTCAATCA CAAAATTTT AAGTCGCTAA CCAACGTTAC 3780
R A F A R E N F Q S Q K F Q V A N Q R Y

ACAGATACTT CAACTGGTCT TTTTAAATTA ACAGGGCTAA CAGAACCACT TTTCGTTCAA 3840
T D T S T G L F K L T G L T E P L F V Q

ATTATTATTG CAATGATTGT GGCTATCGTT TGGTTTGCTT TGGATCCCTT ACAAAGAGGT 3900
I I I A M I V A I V W F A L D P L Q R G

GCTATTAAAA TAGGGGATTT AGTTGCTTTT ATCGAATATA GCTTCCATGC TCTCTTTTCA 3960
A I K I G D L V A F I E Y S F H A L F S

TTTTTGCTAT TTGCCAATCT TTTTACTATG TATCCTCGTA TGGTGGTATC AAGCCATCGT 4020
F L L F A N L F T M Y P R M V V S S H R

ATTAGAGAGG TGATGGATAT GCCAATCTCT ATCAATCCTA ATGCCGAAGG TGTTACGGAT 4080
I R E V M D M P I S I N P N A E G V T D

ACGAAACTTA AAGGGCATT AGAATTTGAT AATGTAACAT TCGCTTATCC AGGAGAAACA 4140
T K L K G H L E F D N V T F A Y P G E T

GAGAGTCCCG TTTTGCATGA TATTTCTTTT AAAGCTAAGC CTGGAGAAAC AATTGCTTTT 4200
E S P V L H D I S F K A K P G E T I A F

ATTGGTTCAA CAGGTTTCAGG AAAATCTTCT CTTGTTAATT TGATTCCACG TTTTATGAT 4260
I G S T G S G K S S L V N L I P R F Y D

GTGACACTTG GAAAAATCTT AGTAGATGGA GTTGATGTAA GAGATTATAA CCTTAAATCA 4320
V T L G K I L V D G V D V R D Y N L K S

CTTCGCCAAA AGATTGGATT TATCCCCCAA AAAGCTCTTT TATTTACAGG GACAATAGGA 4380
L R Q K I G F I P Q K A L L F T G T I G

GAGAATTTAA AATATGGAAA AGCTGATGCT ACTATTGATG ATCTTAGACA AGCGGTTGAT 4440
E N L K Y G K A D A T I D D L R Q A V D

ATTTCTCAAG CTAAAGAGTT TATTGAGAGT CACCAAGAAG CCTTTGAAAC GCATTTAGCT 4500
I S Q A K E F I E S H Q E A F E T H L A

GAAGGTGGGA GCAATCTTTC TGGGGGTCAA AAACAACGGT TATCTATTGC TAGGGCTGTT 4560
E G G S N L S G G Q K Q R L S I A R A V

GTAAAGATC CAGATTTATA TATTTTTGAT GATTCAATTT CTGCTCTCGA TTATAAGACA 4620
V K D P D L Y I F D D S F S A L D Y K T

GACGCTACTT TAAGAGCGCG TCTAAAAGAA GTAACCGGTG ATTCTACAGT TTTGATAGTT 4680
D A T L R A R L K E V T G D S T V L I V

GCTCAAAGGG TGGGTACGAT TATGGATGCT GATCAGATTA TTGTCCTTGA TGAAGGCGAA 4740
A Q R V G T I M D A D Q I I V L D E G E

ATTGTCGGTC GTGGTACCCA CGCTCAATTA ATAGAAAATA ATGCTATTTA TCGTGAAATC 4800
I V G R G T H A Q L I E N N A I Y R E I

GCTGAGTCAC AACTGAAGAA CCAAACTTA TCAGAAGGAG AGTGATTGTA TGAGAAAAAA 4860
A E S Q L K N Q N L S E G E M R K K
|---->

ATCTGTTTTT TTGAGATTAT GGTCTTACCT AACTCGCTAC AAAGCTACTC TTTTCTTAGC 4920
S V F L R L W S Y L T R Y K A T L F L A

GATTTTTTTG AAAGTTTAT CTAGTTTAT GAGTGTTCTG GAGCCTTTTA TTTTAGGGTT 4980
I F L K V L S S F M S V L E P F I L G L

AGCGATAACA GAGTTGACTG CTAACCTTGT TGATATGGCT AAGGGAGTTT CTGGGGCAGA 5040
A I T E L T A N L V D M A K G V S G A E

ATTGAACGTT CCTTATATTG CTGGTATTTT GATTATTTAT TTTTTCAGAG GTGTTTTCTA 5100
L N V P Y I A G I L I I Y F F R G V F Y

TGAATTAGGT TCTTATGGCT CAAATT (SEQ ID NO:7) 5126
E L G S Y G S N

FIG. 2a

NFDIETTTFE	AMKKHASLLE	KISVERSFIE	FDKLLLAPYW	RKGMLALIDS	50
HAFNYLPCLK	NRELQLSAFL	SQDKDFLFE	TSEQAWASLI	LSMEVEHTKT	100
FLKKWKTSTH	FQKDVEHIVD	VYRIREQMGL	AKEHLYRYGK	TIIKQAEGER	150
KARGLMVDFE	KIEQLDSELA	IHDRHEIVVN	GGTLIKKLG	KPGPQMGDII	200
SQIELAIVLG	QLINEEEAIL	HFVKQYLM	(SEQ ID NO:8)		229

FIG. 2b

MSDFLVDGLT	KSVGDKTVFS	NVSFIIHSLD	RIGIIGVNGT	GKTTLLDVIS	50
GELGFDGDRS	PFSSANDYKI	AYLKQEPDFD	DSQTILDTVL	SSDLREMAI	100
KEYELLLNHY	EESKQSRLEK	VMAEMDSLDA	WSIESEVKTV	LSKLGITDLQ	150
LSVGELSGGL	RRRVQLAQVL	LNDADLLLLD	EPTNHLIDIT	IAWLTNFLKN	200
SKKTVLFITH	DRYFLDNVAT	RIFELDKAQI	TEYQGNQDY	VRLRAEQDER	250
DAASLHKKKQ	LYKQELAWMR	TQPQARATKQ	QARINRFQNL	KNDLHQTSDT	300
SDLEMTFETS	RIGKKVINFE	NVSFSYPDKS	ILKDFNLLIQ	NKDRIGIVGD	350
NGVGKSTLLN	LIVQDLQPDS	GNVSIGETIR	VGYFSQQLHN	MDGSKRVINY	400
LQEVADDEVKT	SVGTTSVTEL	LEQFLFPRST	HGTQIAKLSG	GEKKRLYLLK	450
ILIEKPNVLL	LDEPTNDLDI	ATLTVLENFL	QGFGGPVITV	SHDRYFLDKV	500
ANKIIAFEDN	DIREFFGNYT	DYLDEKAFNE	QNNEVISKKE	STKTSREKQS	550
RKRMSYFEKQ	EWATIEDDIM	ILENTITRIE	NDMQTCGSDF	TRLSDLQKEL	600
DAKNEALLEK	YDRYEYLSEL	DT	(SEQ ID NO:9)		622

FIG. 2c

MIIRPIIKND	DQAVAQLIRQ	SLRAYDLDP	DTAYSDPHLD	HLTSYYEKIE	50
KSGFFVIEER	DEIIGCGGFG	PLKNLIAEMQ	KVYIAERFRG	KGLATDLVKM	100
IEVEARKIGY	RQLYLETAST	LSRATAVYKH	MGYCALSQPI	ANDQGHTAMD	150
IWMIKDL	(SEQ ID NO:10)				157

FIG. 2d

MAYIWSYLKR	YPNWLWLDLL	GAMLFVTVIL	GMPTALAGMI	DNGVTKGDRT	50
GVYLTWFIME	IFVVLGIIGR	ITMAYASSRL	TTTMIRDMRN	DMYAKLQEYS	100
HHEYEQIGVS	SLVTRMTSDT	FVLMQFAEMS	LRLGLVTPMV	MIFSVVMILI	150
TSPSLAWLVA	VAMPLLVGVV	LYVAIKTKPL	SERQQTMLDK	INQYVRENLT	200
GLRVVRA FAR	ENFQSQKFQV	ANQRYTDTST	GLFKLTGLTE	PLFVQIIIAM	250
IVAIVWFALD	PLQRGAIKIG	DLVAFIEYSF	HALFSFLLFA	NLFTMYPRMV	300
VSSHRIREVM	DMPISINPNA	EGVTDTKLKG	HLEFDNVTFA	YPGETESPVL	350
HDISFKAKPG	ETIAFIGSTG	SGKSSLVNLI	PRFYDVTLGK	ILVDGVDVRD	400
YNLKSLRQKI	GFIPQKALLF	TGTIGENLKY	GKADATIDDL	RQAVDISQAK	450
EFIESHQEAF	ETHLAEGGSN	LSGGQKQRLS	IARAVVKDPD	LYIFDDSFSA	500
LDYKTDATLR	ARLKEVTGDS	TVLIVAQRVG	TIMDADQIIV	LDEGEIVGRG	550
THAQLIENNA	IYREIAESQL	KNQNLSEGE	(SEQ ID NO:11)		579

FIG. 2e

MRKKS VFLRL	WSYLTRYKAT	LFLAIFLKVL	SSFMSVLEPF	ILGLAITELT	50
ANLVDMAGV	SGAELNVPYI	AGILIIYFFR	GVFYELGSYG	SN	92
(SEQ ID NO:12)					

FIG. 2f

AATTTGGAAG TGCTCTATCA ACAGTTGAAG TAAAGGAGAT TATTAGTGAA GAAAACATAT 60
F G S A L S T V E V K E I I S E E N I W
---->
GGTTATATCG GCTCAGTTGC TGCCATTTTA CTAGCTACTC ATATTGGAAG TTACCAACTT 120
L Y R L S C C H F T S Y S Y W K L P T W
GGTAAGCATC ATATGGGTCT AGCAACAAAG GACAATCAGA TTGCCTATAT TGATGACAGC 180
M G L A T K D N Q I A Y I D D S
|---->
AAAGGTAAGG CAAAAGCCCC TAAAACAAAC AAAACGATGG ATCAAATCAG TGCTGAAGAA 240
K G K A K A P K T N K T M D Q I S A E E
GGCATCTCTG CTGAACAGAT CGTAGTCAAA ATTACTGACC AAGGCTATGT GACCTCACAC 300
G I S A E Q I V V K I T D Q G Y V T S H
GGTGACCATT ATCATTTTTA CAATGGGAAA GTTCCTTATG ATGCGATTAT TAGTGAAGAG 360
G D H Y H F Y N G K V P Y D A I I S E E
TTGTTGATGA CGGATCCTAA TTACCGTTTT AAACAATCAG ACGTTATCAA TGAAATCTTA 420
L L M T D P N Y R F K Q S D V I N E I L
|---->
GACGGTTACG TTATTAAAGT CAATGGCAAC TATTATGTTT ACCTCAAGCC AGGTAGTAAG 480
D G Y V I K V N G N Y Y V Y L K P G S K
CGCAAAAACA TTCGAACCAA ACAACAAATT GCTGAGCAAG TAGCCAAAGG AACTAAAGAA 540
R K N I R T K Q Q I A E Q V A K G T K E
GCTAAAGAAA AAGGTTTAGC TCAAGTGGCC CATCTCAGTA AAGAAGAAGT TGCGGCAGTC 600
A K E K G L A Q V A H L S K E E V A A V
AATGAAGCAA AAAGACAAGG ACGCTATACT ACAGACGATG GCTATATTTT TAGTCCGACA 660
N E A K R Q G R Y T T D D G Y I F S P T
GATATCATTG ATGATTTAGG AGATGCTTAT TTAGTACCTC ATGGTAATCA CTATCATTAT 720
D I I D D L G D A Y L V P H G N H Y H Y
ATTCCTAAAA AGGATTTGTC TCCAAGTGAG CTAGCTGCTG CACAAGCCTA CTGGAGTCAA 780
I P K K D L S P S E L A A A Q A Y W S Q
AAACAAGGTC GAGGTGCTAG ACCGTCTGAT TACCGCCCGA CACCAGCCCC AGGTCGTAGG 840
K Q G R G A R P S D Y R P T P A P G R R
AAAGCCCCAA TTCCTGATGT GACGCCTAAC CCTGGACAAG GTCATCAGCC AGATAACGGT 900
K A P I P D V T P N P G Q G H Q P D N G
GGCTATCATC CAGCGCCTCC TAGGCCAAAT GATGCGTCAC AAAACAAACA CCAAAGAGAT 960
G Y H P A P P R P N D A S Q N K H Q R D
GAGTTTAAAG GAAAAACCTT TAAGGAACTT TTAGATCAAC TACACCGTCT TGATTTGAAA 1020
E F K G K T F K E L L D Q L H R L D L K
TACCGTCATG TGGAAGAAGA TGGGTTGATT TTTGAACCGA CTCAAGTGAT CAAATCAAAC 1080
Y R H V E E D G L I F E P T Q V I K S N
GCTTTTGGGT ATGTGGTGCC TCATGGAGAT CATTATCATA TTATCCCAAG AAGTCAGTTA 1140
A F G Y V V P H G D H Y H I I P R S Q L
TCACCTCTTG AAATGGAATT AGCAGATCGA TACTTAGCTG GCCAAACTGA GGACAATGAC 1200
S P L E M E L A D R Y L A G Q T E D N D
TCAGGTTTCAG AGCACTCAAA ACCATCAGAT AAAGAAGTGA CACATACCTT TCTTGGTCAT 1260

S G S E H S K P S D K E V T H T F L G H
CGCATCAAAG CTTACGGAAA AGGCTTAGAT GGTAAACCAT ATGATACGAG TGATGCTTAT 1320
R I K A Y G K G L D G K P Y D T S D A Y
GTTTTAGTA AAGAATCCAT TCATTCAGTG GATAAATCAG GAGTTACAGC TAAACACGGA 1380
V F S K E S I H S V D K S G V T A K H G
GATCATTTCC ACTATATAGG ATTTGGAGAA CTTGAACAAT ATGAGTTGGA TGAGGTCGCT 1440
D H F H Y I G F G E L E Q Y E L D E V A
AACTGGGTGA AAGCAAAAGG TCAAGCTGAT GAGCTTGCTG CTGCTTTGGA TCAGGAACAA 1500
N W V K A K G Q A D E L A A A L D Q E Q
GGCAAAGAAA AACCACTCTT TGACACTAAA AAAGTGAGTC GCAAAGTAAC AAAAGATGGT 1560
G K E K P L F D T K K V S R K V T K D G
AAAGTGGGCT ATATGATGCC AAAAGATGGT AAGGACTATT TCTATGCTCG TGATCAACTT 1620
K V G Y M M P K D G K D Y F Y A R D Q L
GATTTGACTC AGATTGCCTT TGCCGAACAA GAACTAATGC TTAAAGATAA GAAGCATTAC 1680
D L T Q I A F A E Q E L M L K D K K H Y
CGTTATGACA TTGTTGACAC AGGTATTGAG CCACGACTTG CTGTAGATGT GTCAAGTCTG 1740
R Y D I V D T G I E P R L A V D V S S L
CCGATGCATG CTGGTAATGC TACTTACGAT ACTGGAAGTT CGTTTGTTAT CCCACATATT 1800
P M H A G N A T Y D T G S S F V I P H I
GATCATATCC ATGTCGTTCC GTATTCATGG TTGACGCGCG ATCAGATTGC AACAGTCAAG 1860
D H I H V V P Y S W L T R D Q I A T V K
TATGTGATGC AACACCCCGA AGTTCGTCCG GATGTATGGT CTAAGCCAGG GCATGAAGAG 1920
Y V M Q H P E V R P D V W S K P G H E E
TCAGGTTCCG TCATTCCAAA TGTTACGCCT CTTGATAAAC GTGCTGGTAT GCCAAACTGG 1980
S G S V I P N V T P L D K R A G M P N W
CAAATTATCC ATTCTGCTGA AGAAGTTCAA AAAGCCCTAG CAGAAGGTCG TTTTGCAACA 2040
Q I I H S A E E V Q K A L A E G R F A T
CCAGACGGCT ATATTTTCGA TCCACGAGAT GTTTTGGCCA AAGAACTTT TGTATGGAAA 2100
P D G Y I F D P R D V L A K E T F V W K
GATGGCTCCT TTAGCATCCC AAGAGCAGAT GGCAGTTCAT TGAGAACCAT TAATAATCT 2160
D G S F S I P R A D G S S L R T I N K S
GATCTATCCC AAGCTGAGTG GCAACAAGCT CAAGAGTTAT TGGCAAAGAA AAATACTGGT 2220
D L S Q A E W Q Q A Q E L L A K K N T G
GATGCTACTG ATACGGATAA ACCCAAAGAA AAGCAACAGG CAGATAAGAG CAATGAAAAC 2280
D A T D T D K P K E K Q Q A D K S N E N
CAACAGCCAA GTGAAGCCAG TAAAGAAGAA AAAGAATCAG ATGACTTTAT AGACAGTTTA 2340
Q Q P S E A S K E E K E S D D F I D S L
CCAGACTATG GTCTAGATAG AGCAACCCTA GAAGATCATA TCAATCAATT AGCACAAAAA 2400
P D Y G L D R A T L E D H I N Q L A Q K
GCTAATATCG ATCCTAAGTA TCTCATTTTC CAACCAGAAG GTGTCCAATT TTATAATAAA 2460
A N I D P K Y L I F Q P E G V Q F Y N K

AATGGTGAAT TGGTAACTTA TGATATCAAG ACACTTCAAC AAATAAACCC TTAACCAAAA 2520
 N G E L V T Y D I K T L Q Q I N P
 GAAGATCTCA TTGTTAAAGC ACTGCTTTGT CAAAGCAAGT TACGGTGATT TTGAAGTCAT 2580
 TCTATGTAAC GAGTAGTGAT AAAAGTTGGA TAATAGCGGT TTTCTTTTGC AAAGAAATGG 2640
 TATCCATGTT AGAATAGTAA AAAAAGAGGA GGATTCTTGG ACTAATGTCA AATAAGTAGA 2700
 CAGAAACTG TGTTATTTTA TTGCGTTAAA ATAATTTTCT TCTTTCTGAT TAGGGGTTAG 2760
 .K I A N F Y N E E K Q N P T L
 TCCTAGATTA GCCGTATGTG GGTGTAATT GTTATAAAAA TTCTCAATGT ATTCAAAGCA 2820
 G L N A T H P N Y N N Y F N E I Y E F C
 GTCTAATTGA ACCTGTTTGA TATTTTGATA ATGTTTTCGG TTGATTGTGC TATGCTTTAA 2880
 D L Q V Q K I N Q Y H K R N I Q R H K L
 AACTTGAAA AATGCTTCAG TTACGGCATT ATCATAAGGA TATCCAGGAT TAGAAAAAGA 2940
 Y K F F A E T V A N D Y P Y G P N S F S
 ATGCATGATA TTGGCACTGC ACCCTAATAG TGAGACGCAA GAAAAACACT TTTAGGCAAT 3000
 H M A I
 <----|
 CAGTTTCTG TACTGTACAG GCGACTGGTC GTTAAATCTC TGTGGAATTC TAGTTTCATT 3060
 L K R Y Q V P S Q D N L R Q Q I R T E N
 ATAAAATGTA ATGTAATTTT TAACAATATT TGTATACTA TCTTGTTGT ATTTTCTCCT 3120
 Y F T I Y N K V I N T I S D K N Y K R R
 ATTATGAAA TAAAAGGTTT CAGTCTTTAG GACGGTGTGA AACCATTCAA TACAGGCATT 3180
 N H F Y F T E T K L V T H F W E I C A N
 ATCTGCAGGT GTTCCTTTTC GAGACATTGA GCGGATAATG TCTTTTCCG TGCAAGCCTG 3240
 D A P T G K R S M S R I I D K E T C A Q
 GTAGTAAGCC ATAGAAGTAT ACACTGAGCC TTGGTCACTG TGTAAGATTG CTCCTTTATT 3300
 Y Y A M
 <----|
 TAGGCAATTT TAACTGATTA AGGGTGTCTA GTACAAAATC CGTGTCTGA CAATCTGAGA 3360
 K P L K L Q N L T D L V F D T D Q C D S
 TAGTGTAAGC TATAATTTCT CGGTTATAGA GATTCATAAT TGATGAGAGA TACAATTTAC 3420
 I T Y A I I E R N Y L N M I S S L Y L K
 AGTTACCGAA ATATAGGTAG GTAATATCTG TTACGAGCTT TTCCTTAGGC TTATCGGCAT 3480
 C N G F Y L Y T I D T V L K E K P K D A
 GGAAATCCCG ACTCAATTTA TTATCTGTGA AATAATAAGC TTTACCCAAA TTGGGAACTT 3540
 H G D R S L K N D T L Y Y A K G L N P V
 TCTTGGTACG TGTCCGACAA AGCCAGCCAT TATTTTTCAT GATACGATAG ACTTTCTTTG 3600
 K K T R T R C L W G N N K M I R Y V K K
 TATTAACAGT CAATCCGTGG ATTTTGTGA GCAATCGTGT AATGGTACGA TAGCCATAAA 3660
 T N V T L G H I K K L L R T I T R Y G Y
 TAAAGTGATT CTCCATACAG AGCTGTTCAA TTAATTCAAT AAGGTCATCT TTTTGTGCGG 3720
 I F H N E M
 <----|

CTTCTCATAC TCCTTTTTCC AACGGTAATA GGTCGACCGC TTGACCTTAA AACAGTCTAG 3780
 AATGAAAAC TATCGGGTAGT TGTTTTTATA GTCTTCCACA AGCTTGATAA GACTTACTTT 3840
 ATCGATTTCC TTATCAAGCC TCGATACTTT TTTAAGAGGT CAACCTGTAA TTGTAATTGT 3900
 I S K R I L G R Y K K L L D V Q L Q L Q
 TCCACTTCAG ACAGATGTTT CAAGCCTTTA CCGTAGGTAT ATTGCTTGCC AACACCTTGA 3960
 E V E S L H E L G K G Y T Y Q K G V G Q
 TGAAAACGAT AAAGCTCCTC GTTTTTCGTAC CATTTTCATCC AAGTATAGAT TTGACTATTA 4020
 H F R Y L E E N E Y W K M W T Y I Q S N
 TTTTGTATGC CTAAAGTCTC CATAATAACT CTGTTAGACT TGCCTGCTTT CTTTCATATCG 4080
 N K I G L T E M I V R N S K G A K K M D
 ATGCAAGCCA GCTTAGTTTC CCATGAATAT GCTTTTTTAA CCATAATAAA ACATTCCTGT 4140
 I C A L K T E W S Y A K K V M
 TTCTAGTTTA CTAAATTTCA ACAGGAGTGT TTTTCTTTTG TCTCATTTTA GGGATTCAGT 4200
 GCCTATTGTT GTCATCAATT ATTTTCTAA ATTCCCCGGA CTAAATTGT GACCCTTGGT 4260
 CGGAATGAAA GAGAAGTGTT CCTTCAATCT TTCTTTTATT AAGTGAAAAG GCAACACTTT 4320
 TCTGTACAAC ATTTATAAAG TGTTTTTCTA GGCAATTAAT CTTTGTAGTCA TTGGTGTTTG 4380
 . A I L R K T M P T Q
 GTAGTTGAGA CTACCATGAA TGCGGTGGTA ATTCCACCAA TGAACATAGT CTTTAGTCTT 4440
 Y N L S G H I R H Y N W W H V Y D K T K
 AAGAGCTAGT TCTTCCAGCA ATTGAAAGGT TTCTTGATAA ACAAATTCAA TTTTGAAAGC 4500
 L A L E E L L Q F T E Q Y V F E I K F A
 ACGATACGTA CTTTCAGCTA CGGCATTGTC ATAAGGATAA CCAGCCTGAC TAAGCGAACG 4560
 R Y T S E A V A N D Y P Y G A Q S L S R
 TGTGATTCCA AAGGCTTCCA ATATTTTCATC AATTAAGTGA TTATCAAACCT CTTTGCCACG 4620
 T I G F A E L I E D I L Q N D F E K G R
 ATCTGAATGG AACATCTTGA CTTTGGTCAG GCGGTAAGGG ATGCTTTGTA TGGCTTGCTT 4680
 D S H F M K V K T L A Y P I S Q I A Q K
 AACGAGTTCA GCGGTCTTGT GCCAACCAAG AGACAGGCCG ATGATTTTAC GGTGTATAG 4740
 V L E A T K H W G L S L G I I E R N Y L
 GTCAATGATG AGGCAAACAT AAGCCCAACG ATTGCCTACA CGAACATAGG TTAAGTCAGT 4800
 D I I L C V Y A W R N G V R V Y T L D T
 GACTAAGGCT TGTAAGTGGT TTTCTTGCTT AAATTGCCTG TCTAAGTGGT TGGGAATAGG 4860
 V L A Q L P R E Q K F Q R D L H N P I P
 GGCTTCATTC TTGCCTCTAG AATGTGGTTT GAAGGTGGCT TTCTGATAAA CAGAAACCAA 4920
 A E N K G R S H P K F T A K Q Y V S V L
 ATTGAGTCGC TTCATAATGC GTCGAATCCG ACGACGTGAA AGTGTGATAC CTTGCTTATT 4980
 N L R K M I R R I R R R S L T I G E N N
 CAAGCATATT TTGATTTTTC TGGATCCGTA TCTAGACTCG CTATCGAGAA AAATTCTTTT 5040
 L C I K I K R S G Y R S E S D L F I R K

AATAGTTTCT TCAAACCTCCG TTTCAGATAC TGACTCCACG GCTTGATAGT AATAACTTGA 5100
I T E E F E T E S V S E V A Q Y Y Y S S
GTGTGGCATA TTCAGCCAGC GACACATCTT TGAAATGCTG TATTTATCCT TATTAGCAGT 5160
H P M N L W R C M K S I S Y K D K N A T
GATTATTTCC CTTTTGTGC CATAATCACC GCTGCTTGCT TTAGGATATC TAATT 5215
I I E R K T G Y D G S S A K P Y R I
(SEQ ID NO:13) <----|

FIG. 3a

FGSALSTVEV KEIISEENIW LYRLSCCHFT SYSYWKLPWT 40
(SEQ ID NO:14)

FIG. 3b

MGLATKDNQI AYIDDSKGKA KAPKTNKTMD QISAEEGISA EQIVVKITDQ 50
GYVTSHGDHY HFYNGKVPYD AIISEELMT DPNYRFKQSD VINEILDGYV 100
IKVNGNYVYVY LKPGSKRKNI RTKQQIAEQV AKGTKEAKEK GLAQVAHLSK 150
EEVAAVNEAK RQGRYTTDDG YIFSPTDIID DLGDAYLVPH GNHYHYIPKK 200
DLSPSELAAA QAYWSQKQGR GARPSDYRPT PAPGRRKAPI PDVTPNPGQG 250
HQPDNNGGYHP APPRPNDASQ NKHQORDEFKG KTFKELLDQL HRLDLKYRHV 300
EEDGLIFEPT QVIKSNAFGY VVPHGDHYHI IPRSQLSPLE MELADRYLAG 350
QTEDNDSGSE HSKPSDKEVT HTFLGHRIKA YGKGLDGKPY DTSDAYVFSK 400
ESIHSVDKSG VTAKHGDHFEH YIGFGELEQY ELDEVANWVK AKGQADELAA 450
ALDQEQGKEK PLFDTKKVSR KVTKDGVKGY MMPKDGKDYG YARDQLDLTQ 500
IAFAEQELML KDKKHRYDI VDTGIEPRLA VDVSSLPMHA GNATYDTGSS 550
FVIPHIDHIH VVPYSWLTRD QIATVKYVMQ HPEVRPDVWS KPGHEESGSV 600
IPNVTPLDKR AGMPNWQIIH SAEVQKALA EGRFATPDGY IFDPRDVLAK 650
ETFWKDGSE SIPRADGSSL RTINKSDLSQ AEWQQAQELL AKKNTGDATD 700
TDKPKEKQQA DKSNNQOPS EASKEEKESD DFIDSLPDYG LDRATLEDHI 750
NQLAQKANID PKYLIFQPEG VQFYKNKNGEL VTYDIKTLQQ INP 793
(SEQ ID NO:15)

FIG. 3c

MTDPNYRFKQ	SDVINEILDG	YVIKVNGNYY	VYLKPGSKRK	NIRTKQQIAE	50
QVAKGTKEAK	EKGLAQVAHL	SKEEVAAVNE	AKRQGRTTDD	DGYIFSPTDI	100
IDDLGDAYLV	PHGNHYHYIP	KKDLSPSELA	AAQAYWSQKQ	GRGARPSDYR	150
PTPAPGRRKA	PIPDVTPNPG	QGHQPDNGGY	HPAPPRPND	SQNKHQDEF	200
KGKTFKELLD	QLHRLDLKYR	HVEEDGLIFE	PTQVIKSNAF	GYVVPBGDHY	250
HIIPRSQLSP	LEMELADRYL	AGQTEDNDSD	SEHSKPSDKE	VTHTFLGHRI	300
KAYGKGLDGK	PYDTSDAYVF	SKESIHSVDK	SGVTAKHGDH	FHYIGFGELE	350
QYELDEVANW	VKAKGQADEL	AAALDQEQGK	EKPLFDTKKV	SRKVTKDGKV	400
GYMMPKDGD	YFYARDQLDL	TQIAFAEQEL	MLKDKKHRY	DIVDTGIEPR	450
LAVDVSSLPM	HAGNATYDTG	SSFVIPHIDH	IHVVPYSWLT	RDQIATVKYV	500
MQHPEVRPDV	WSKPGHEESG	SVIPNVTPLD	KRAGMPNWQI	IHSAAEVQKA	550
LAEGRFATPD	GYIFDPRDVL	AKETFWWKDG	SFSIPRADGS	SLRTINKSDL	600
SQAEWQQAQE	LLAKKNTGDA	TDTDKPKEKQ	QADKSNENQQ	PSEASKEEKE	650
SDDFIDSLPD	YGLDRATLED	HINQLAQKAN	IDPKYLIFQP	EGVQFYNKNG	700
ELVTYDIKTL	QQINP	(SEQ ID NO:16)			715

FIG. 3d

MHSFSNPGYP	YDNAVTEAFF	KYLKHRQINR	KHYQNIQVQ	LDCFYIENF	50
YNNYNPHTAN	LGLTPNQKEE	NYFNAIK	(SEQ ID NO:17)		77

FIG. 3e

MAYYQACTEK	DIIRMSRKG	TPADNACIEW	FHTVLKTETF	YFHNRRKYNK	50
DSITNIVKNY	ITFYNETRIQ	QRLNDQSPVQ	YRKLIA	(SEQ ID NO:18)	86

FIG. 3f

MENHFIYGYR	TITRLLKKIH	GLTVNTKKVY	RIMKNNGWLC	RTRTKKVPNL	50
GKAYYLTDNK	LSRDFHADKP	KEKLVTDITY	LYFGNCKLYL	SSIMNLYNRE	100
IIAYTISDCQ	DTDFVLDTLN	QLKLPK	(SEQ ID NO:19)		126

FIG. 3g

MVKKAYSWET KLACIDMKKA GKSNRVIMET LGIKNNSQIY TWMKWYENEE 50
 LYRFHQGVGK QYTYGKGLEH LSEVEQLQLQ VDLLKKYRGL IRKSIK 96
 (SEQ ID NO:20)

FIG. 3h

IRYPKASSGD YGTKREIITA NKDKYSISKM CRWLNMPHSS YYYQAVESVS 50
 ETEFEETIKR IFLDSESRYG SRKIKICLNN EGITLSRRRI RRIMKRLNLV 100
 SVYQKATFKP HSRGKNEAPI PNHLDRQFKQ ERPLQALVTD LTYVRVGNRW 150
 AYVCLIIDLY NREIIGLSLG WHKTAELVKQ AIQSIPYALT KVKMFHSDRG 200
 KEFDNQLIDE ILEAFGITRS LSQAGYPYDN AVAESTYRAF KIEFVYQETF 250
 QLEELALKT KDYVHWWNYH RIHGSLNYQT PMTKRLIA (SEQ ID NO:21) 288

FIG. 3i

AATTGAAAG CAGAATTATC TGTAGAAGAT GAGCAATATA CAGCAACAGT TTATGGTAAA 60
 N L K A E L S V E D E Q Y T A T V Y G K
 ---->
 TCTGCTCATG GTTCAACACC ACAAGAAGGT GTTAATGGGG CGACTTATTT AGCTCTTTAT 120
 S A H G S T P Q E G V N G A T Y L A L Y
 CTAAGTCAAT TTGATTTTGA AGGTCCTGCT CGTGCTTTCT TAGATGTTAC AGCCAACATT 180
 L S Q F D F E G P A R A F L D V T A N I
 ATTCACGAAG ACTTCTCAGG TGA AAAACTT GGAGTAGCTT ATGAAGATGA CTGTATGGGA 240
 I H E D F S G E K L G V A Y E D D C M G
 CCATTGAGCA TGAATGCAGG TGTCTTCCAG TTTGATGAAA CTAATGATGA TAATACTATC 300
 P L S M N A G V F Q F D E T N D D N T I
 GCTCTTAATT TCCGTTACCC ACAAGGGACA GATGCTAAAA CTATCCAAAC TAAGCTTGAG 360
 A L N F R Y P Q G T D A K T I Q T K L E
 AAACCTAACG GAGTTGAAAA AGTGACTCTT TCTGACCATG AACACACACC AACTATGTA 420
 K L N G V E K V T L S D H E H T P H Y V
 CCTATGGACG ATGAATTAGT ATCAACCTTA CTAGCTGTCT ATGAAAAGCA AACTGGTCTT 480
 P M D D E L V S T L L A V Y E K Q T G L
 AAAGGACATG AACAGGTTAT TGGTGGTGGG ACATTTGGTC GCTTACTTGA ACGGGGTGTT 540
 K G H E Q V I G G G T F G R L L E R G V
 GCATACGGTG CCATGTTCCC AGGAGATGAA AACACTATGC ATCAAGCTAA TGAGTACATG 600
 A Y G A M F P G D E N T M H Q A N E Y M
 CCTTTAGAAA ATATTTTCCG TTCGGCTGCT ATCTACGCAG AAGCTATCTA TGAATTAATC 660

P L E N I F R S A A I Y A E A I Y E L I
 AAATAAAATA ATCCTTAAAC TAAATATGTG ATCAATGATA AAGGGTGGTG AAGACATGAA 720
 K .
 AGTGTCTTTG CCTCTTTTCA TAAGGTTAGA TTTGGAGACT TTATGACTGA CTTGGAAAAA 780
 M T D L E K
 |---->
 ATTATTAAAG CAATAAAAAG TGATTCACAG AATCAAAATT ATACAGAAAA TGGTATTGAT 840
 I I K A I K S D S Q N Q N Y T E N G I D
 CCTTTGTTTG CTGCTCCTAA AACAGCTAGG ATCAATATTG TTGGCCAAGC ACCTGGTTTA 900
 P L F A A P K T A R I N I V G Q A P G L
 AAAACTCAAG AAGCAAGACT CTATTGGAAA GATAAATCTG GAGATCGTCT ACGCCAGTGG 960
 K T Q E A R L Y W K D K S G D R L R Q W
 CTTGGAGTTG ATGAAGAGAC ATTTTACCAT TCTGGAAAAT TTGCTGTTTT ACCTTTAGAT 1020
 L G V D E E T F Y H S G K F A V L P L D
 TTTTATTACC CAGGCAAAGG AAAATCAGGA GATTTACCCC CTAGAAAAGG TTTTGCGGAG 1080
 F Y Y P G K G K S G D L P P R K G F A E
 AAATGGCACC CTCTTATTTT AAAAGAAATG CCTAATGTTC AATTGACCTT GCTAGTTGGT 1140
 K W H P L I L K E M P N V Q L T L L V G
 CAGTATGCTC AGAAATATTA TCTTGAAGC TCCGCACATA AAAATCTAAC AGAAACAGTT 1200
 Q Y A Q K Y Y L G S S A H K N L T E T V
 AAAGCTTACA AAGACTATCT ACCCGATTAT TTACCCCTGG TTCACCCATC ACCGCGAAAT 1260
 K A Y K D Y L P D Y L P L V H P S P R N
 CAAATTGGC TAAAGAAGAA TCCATGGTTT GAAAAAGATC TAATCGTTGA TTTACAAAAG 1320
 Q I W L K K N P W F E K D L I V D L Q K
 ATAGTAGCAG ATATTTTAAA AGATTAAAGGA TAGGAGTTGG TATGAGAGAT AATCATCTAC 1380
 I V A D I L K D . M R D N H L H
 |---->
 ACACGTATTT TTCCTATGAT TGTCAAACGG CATTGAGGA CTATATTAAT GGTTTTACAG 1440
 T Y F S Y D C Q T A F E D Y I N G F T G
 GTGAATTTAT CACGACAGAA CATTTTGATT TATCAAATCC TTACACCGGT CAAGACGATG 1500
 E F I T T E H F D L S N P Y T G Q D D V
 TTCCTGATTA TAGTGCTTAT TGTCAAAAA TAGATTATCT TAATCAGAAA TATGGAAATC 1560
 P D Y S A Y C Q K I D Y L N Q K Y G N R
 GATTAAAAA AGGAATTGAA ATCGGTTATT TTAAAGATAG GGAATCAGAT ATTTTAGATT 1620
 F K K G I E I G Y F K D R E S D I L D Y
 ATTTAAAAA TAAAGAATTT GATTAAAAC TATTGTCAAT CCATCATAAT GGTAGGTATG 1680
 L K N K E F D L K L L S I H H N G R Y D
 ATTATCTGCA AGAAGAAGCT CTGAAAGTAC CAACAAAGGG AGCTTTTAGC AGATTACTTT 1740
 Y L Q E E A L K V P T K G A F S R L L .
 AATCGTATGG AATTTGCCAT AGGCCGTGTG GAAGCGCACG TTTTAGCTCA CTTTGATTAT 1800
 GGTTCGTA AGTTAACTT AGATGTAGAA GATTAAAAC CGTTTGAAAC GCAATTGAAG 1860
 CGCATTTTCA TAAAGATGTT ATCTAAGGGG TTAGCTTTTG AACTAAATAC CAAATCCCTT 1920

TATCTATATG GGAATGAAAA ACTTTATCGC TATGCTTTAG AGATACTCAA ACAGCTTGGT 1980
 TGTAACAAT ACTCTATAGG CTCTGACGGT CATATTCCTG AACATTTTGT TTATGAATTT 2040
 GATAGACTTC AAGGTCTGCT AAAGGACTAT CAAATTGATG AAAATCATTG GATATGAGGA 2100
 AATTTTGTAT AAAAAAGCTA GGCAATATTG CTTAGCTTTT TTGTAATGCT ATTGATAGTT 2160
 TTAGTGAAAA TTTCAAAAAA ATAAAGAAAT CATTTACTTG TTGCAAGCGC TTGCGTAAAT 2220
 TGTTATGATT TTATTGGTAA CAATTCATTA AAAAAGGAGA ATGATATGAA AAGAAAAGAC 2280
 TTATTGGTG ATAAACAAAC TCAATACAGC ATTAGAAAGT TAAGTGTGG AGTAGCTTCA 2340
 L F G D K Q T Q Y T I R K L S V G V A S
 GTTACAACAG GGGTATGTAT TTTTCTTCAT AGTCCACAGG TATTGCTGA AGAAGTAAGT 2400
 V T T G V C I F L H S P Q V F A E E V S
 GTTCTCCTG CAACTACAGC GATTGCAGAG TCGAATATTA ATCAGGTTGA CAACCAACAA 2460
 V S P A T T A I A E S N I N Q V D N Q Q
 TCTACTAATT TAAAGATGA CATAAACTCA AACTCTGAGA CGGTTGTGAC ACCCTCAGAT 2520
 S T N L K D D I N S N S E T V V T P S D
 ATGCCGGATA CCAAGCAATT AGTATCAGAT GAAACTGACA CTCAAAAGGG AGTGACAGAG 2580
 M P D T K Q L V S D E T D T Q K G V T E
 CCGGATAAGG CGACAAGCCT GCTTGAAGAA AATAAAGGTC CTGTTTCAGA TAAAAATACC 2640
 P D K A T S L L E E N K G P V S D K N T
 TTAGATTTAA AAGTAGCACC ATCTACATTG CAAAATACTC CCGACAAAAC TTCTCAAGCT 2700
 L D L K V A P S T L Q N T P D K T S Q A
 ATAGGTGCTC CAAGCCCTAC CTTGAAAGTA GCTAATCAAG CTCCACGGAT TGAAAATGGT 2760
 I G A P S P T L K V A N Q A P R I E N G
 TACTTTAGGC TACATCTTAA AGAATTGCCT CAAGGTCATC CTGTAGAAAG CACTGGACTT 2820
 Y F R L H L K E L P Q G H P V E S T G L
 TGGATATGGG GAGATGTTGA TCAACCGTCT AGTAATTGGC CAAATGGTGC TATCCCTATG 2880
 W I W G D V D Q P S S N W P N G A I P M
 ACTGATGCTA AGAAAGATGA TTACGGTTAT TATGTTGATT TTAAATTATC TGAAAAACAA 2940
 T D A K K D D Y G Y Y V D F K L S E K Q
 CGAAAACAAA TATCTTTTTT AATTAATAAC AAAGCAGGGA CAAATTTAAG CGGCGATCAT 3000
 R K Q I S F L I N N K A G T N L S G D H
 CATATTCCAT TATTACGACC TGAGATGAAC CAAGTTTGA TTGATGAAAA GTACGGTATA 3060
 H I P L L R P E M N Q V W I D E K Y G I
 CATACTTATC AACCCCTCAA AGAAGGGTAT GTCCGTATTA ACTATTTGAG TTCCTCTAGT 3120
 H T Y Q P L K E G Y V R I N Y L S S S S
 AACTATGACC ACTTATCAGC ATGGCTCTTT AAAGATGTTG CAACCCCYTC AACAACTTGG 3180
 N Y D H L S A W L F K D V A T P S T T W
 CCAGATGGTA GTAATTTTGT GAATCAAGGA CTATATGGAA GGTATATTGA TGTATCACTA 3240
 P D G S N F V N Q G L Y G R Y I D V S L

AAACTAACG CCAAAGAGAT TGGTTTTCTA ATCTTAGATG AAAGTAAGAC AGGAGATGCA 3300
K T N A K E I G F L I L D E S K T G D A

GTGAAAGTTC AACCCAACGA CTATGTTTTT AGAGATTTAG CTAACCATAA CCAAATTTTT 3360
V K V Q P N D Y V F R D L A N H N Q I F

GTAAAAGATA AGGATCCAAA GGTTTATAAT AATCCTTATT ACATTGATCA AGTGCAGCTA 3420
V K D K D P K V Y N N P Y Y I D Q V Q L

AAGGATGCCC AACAAATTGA TTTAACAAGT ATTCAAGCAA GTTTTACAAC TCTAGATGGG 3480
K D A Q Q I D L T S I Q A S F T T L D G

GTAGATAAAA CTGAAATTTT AAAAGAATTG AAAGTGACTG ATAAAAATCA AAATGCTATA 3540
V D K T E I L K E L K V T D K N Q N A I

CAAATTTCTG ATATCACTCT CGATACTAGT AAATCTCTTT TAATAATCAA AGGCGACTTT 3600
Q I S D I T L D T S K S L L I I K G D F

AATCCTA AACGTCATTT CAACATATCT TATAATGGTA ACAATGTCAT GACAAGGCAA 3660
N P K Q G H F N I S Y N G N N V M T R Q

TCTTGGGAAT TTAAAGACCA ACTTTATGCT TATAGTGGAA ATTTAGGTGC AGTTCTCAAT 3720
S W E F K D Q L Y A Y S G N L G A V L N

CAAGATGGTT CAAAAGTTGA AGCCAGCCTC TGGTCACCGA GTGCTGATAG TGTCACTATG 3780
Q D G S K V E A S L W S P S A D S V T M

ATTATTTATG ACAAAGATAA CCAAACAGG GTTGTAGCGA CTACCCCCCT TGTGAAAAT 3840
I I Y D K D N Q N R V V A T T P L V K N

AATAAAGGTG TTTGGCAGAC GATACTTGAT ACTAAATTAG GTATTAAAAA CTATACTGGT 3900
N K G V W Q T I L D T K L G I K N Y T G

TACTATTATC TTTACGAAAT AAAAAGAGGT AAGGATAAGG TTAAGATTTT AGATCCTTAT 3960
Y Y Y L Y E I K R G K D K V K I L D P Y

GCAAAGTCAT TAGCAGAGTG GGATAGTAAT ACTGTTAATG ATGATATTAA AACGGCTAAA 4020
A K S L A E W D S N T V N D D I K T A K

GCAGCTTTTG TAAATCCAAG TCAACTTGGG CCTCAAATT TAAGTTTTGC TAAAATTGCT 4080
A A F V N P S Q L G P Q N L S F A K I A

AATTTTAAAG GAAGACAAGA TGCTGTTATA TACGAAGCAC ATGTAAGAGA CTTCACTTCT 4140
N F K G R Q D A V I Y E A H V R D F T S

GATCGATCTT TGGATGGAAA ATTAAAAAAT CAATTGGTA CCTTTGCAGC CTTTTCAGAG 4200
D R S L D G K L K N Q F G T F A A F S E

AACTAGATT ATTTACAGAA ATTAGGAGTT ACACACATTC AGCTTTTACC GGTATTGAGT 4260
K L D Y L Q K L G V T H I Q L L P V L S

TATTTTATG TTAATGAAAT GGATAAGTCA CGCTCAACAG CTTACACTTC CTCAGACAAT 4320
Y F Y V N E M D K S R S T A Y T S S D N

AATTACAATT GGGGCTATGA CCCACAGAGC TATTTTGCTC TTTCTGGGAT GTATTCAGAG 4380
N Y N W G Y D P Q S Y F A L S G M Y S E

AAACCAAAG ATCCATCAGC ACGTATCGCC GAATTAAAC AATTAATACA TGATATTCAT 4440
K P K D P S A R I A E L K Q L I H D I H

AAACGTGGCA TGGGGGTTAT ACTTGATGTC GTCTATAATC ACACTGCAAA AACTTATCTC 4500
 K R G M G V I L D V V Y N H T A K T Y L
 TTTGAGGATA TAGAACCTAA TTATTATCAC TTTATGAATG AAGATGGTTC ACCAAGAGAA 4560
 F E D I E P N Y Y H F M N E D G S P R E
 AGTTTTGGAG GGGGACGTTT AGGAACCACT CATGCAATGA GTCGTCGTGT TTTGGTTGAT 4620
 S F G G G R L G T T H A M S R R V L V D
 TCCATTAAAT ATCTTACAAG TGAATTTAAA GTTGATGGTT TCCGTTTTGA TATGATGGGA 4680
 S I K Y L T S E F K V D G F R F D M M G
 GATCATGATG CGGCTGCGAT TGAATTAGCT TATAAAGAAG CTAAAGCTAT TAATCCTAAT 4740
 D H D A A A I E L A Y K E A K A I N P N
 ATGATTATGA TTGGTGAGGG CTGGAGAACA TTCCAAGGCG ATCAAGGTCA GCCGGTTAAA 4800
 M I M I G E G W R T F Q G D Q G Q P V K
 CCAGCTGACC AAGATTGGAT GAAGTCAACC GATACAGTTG GCGTCTTTTC AGATGATATT 4860
 P A D Q D W M K S T D T V G V F S D D I
 CGTAATAGCT TGAAATCTGG TTTTCCAAAT GAAGGTACTC CAGCTTTCAT CACAGGTGGC 4920
 R N S L K S G F P N E G T P A F I T G G
 CCACAATCTT TACAAGGTAT TTTTAAAAAT ATCAAAGCAC AACCTGGGAA TTTTGAAGCA 4980
 P Q S L Q G I F K N I K A Q P G N F E A
 GATTCGCCAG GAGATGTGGT GCAGTATATT GCTGCACATG ATAACCTTAC CTTGCATGAT 5040
 D S P G D V V Q Y I A A H D N L T L H D
 GTGATTGCAA AATCAATT (SEQ ID NO:22) 5058
 V I A K S I .

FIG. 4a

NLKAELSVED EQYTATVY GK SAHGSTPQEG VNGATYLALY LSQFDFEGPA 50
 RAFLDVTANI IHEDFSGEKL GVAYEDDCMG PLSMNAGVFQ FDETNDNDNTI 100
 ALNFRYPQGT DAKTIQTKLE KLNGVEKVTL SDHEHTPHYV PMDELVSTL 150
 LAVYEKQTGL KGHEQVIGGG TFGRLLERGV AYGAMFPGDE NTMHQANEYM 200
 PLENIFRSAA IYAEAIYELI K (SEQ ID NO:23) 221

FIG. 4b

MTDLEKIIKA IKSDSQNQNY TENGIDPLFA APKTARINIV GQAPGLKTQE 50
 ARLYWKDKSG DRLRQWLGV D EETFYHSGKF AVLPLDFYYP GKGKSGDLPP 100
 RKGFAEKWHP LILKEMPNVQ LTLVGVQY AQ KYYLGS SAHK NLTETVKAYK 150
 DYLPDYLPV HPSPRNQIWL KKNPWFEKDL IVDLQKIVAD ILKD 194
 (SEQ ID NO:24)

FIG. 4c

MRDNHLHTYF SYDCQTAFED YINGFTGEFI TTEHFDLSNP YTGQDDVPDY 50
SAYCQKIDYL NQKYGNRFKK GIEIGYFKDR ESDILDYLN KEFDLKLLSI 100
HHNGRYDYLO EEALKVPTKG AFSRLL (SEQ ID NO:25) 126

FIG. 4d

MKRKDLFGDK QTQYTIRKLS VGVASVTTGV CIFLHSPQVF AEEVSVSPAT 50
TAIAESNINQ VDNQQSTNLK DDINSNSETV VTPSDMPDTK QLVSEDTDTQ 100
KGVTEPDKAT SLLEENKGPV SDKNTLDLKV APSTLQNTPD KTSQAIGAPS 150
PTLKVANQAP RIENGYFRLH LKELPQGHV ESTGLWIWGD VDQPSSNWP 200
GAIPMTDAKK DDYGYVDFK LSEKQKQIS FLINNKAGTN LSGDHHIPLL 250
RPEMNQVWID EKYGIHTYQP LKEGYVRINY LSSSSNYDHL SAWLFKDVAT 300
PSTTWPDGSN FVNQGLYGRY IDVSLKTNK EIGFLILDES KTGDVAVKVP 350
NDYVFRDLAN HNQIFVKDKD PKVYNNPYI DQVQLKDAQQ IDLTSIQASF 400
TTLDGVDKTE ILKELKVTDK NQNAIQISDI TLDTSKSLI IKGDFNPKQG 450
HFNISYNGNN VMTRQSWEFK DQLYAYSGNL GAVLNQDGSK VEASLWSPSA 500
DSVTMIIYDK DNQNRVVATT PLVKNNKGW QTILDTKLG I KNYTGYYYLY 550
EIKRGKDKVK ILDPYAKSLA EWDSNTVNDD IKTAKAAFN PSQLGPNLS 600
FAKIANFKGR QDAVIYEAHV RDETSRSLD GKLKNQFGTF AAFSEKLDYL 650
QKLGVTIQL LPVLSYFYVN EMDKSRSTAY TSSDNNYNWG YDPQSYFALS 700
GMYSEKPKDP SARIAELKQL IHDHKGGMG VILDVVYNHT AKTYLFEDIE 750
PNYYHFMNED GSPRESFGG RLGTTHAMSR RVLVDSIKYL TSEFKVDGFR 800
FDMMGDHDA AIELAYKEAK AINPNMIMIG EGWRTFQGDQ GQPVKPADQD 850
WMKSTDVGV FSDDIRNSLK SGFPNEGTPA FITGGPQSLQ GIFKNIKAQP 900
GNFEADSPGD VVQYIAAHDN LTLHDVIAK I (SEQ ID NO:26) 931

FIG. 4e

AATTCAAAGT TTGACAGAAG GTCAACTTCG TTCTGATATC CCTGAGTTCC GTGCTGGTGA 60
 I Q S L T E G Q L R S D I P E F R A G D
 ----->
 TACTGTACGT GTTCACGCTA AAGTTGTTGA AGGTACTCGC GAACGTATTC AGATCTTTGA 120
 T V R V H A K V V E G T R E R I Q I F E
 AGGTGTTGTT ATCTCACGTA AAGGTCAAGG AATCTCAGAA ATGTACACAG TACGTAAAAT 180
 G V V I S R K G Q G I S E M Y T V R K I
 TTCTGGTGGT ATCGGTGTAG AGCGTACATT CCCAATTCAC ACTCCTCGTG TTGATAAAAT 240
 S G G I G V E R T F P I H T P R V D K I
 CGAAGTTGTT CGTTATGGTA AAGTACGTCG TGCTAAACTT TACTACTTAC GCGCATTGCA 300
 E V V R Y G K V R R A K L Y Y L R A L Q
 AGGTAAAGCT GCACGTATTA AAGAAATCCG TCGTTAATTT TGATGATCAG ATTTTAAAAA 360
 TGCTTGTTG TTTGAGGATA GTAACATATGT TTTAAACTG GACAACCAAG ACGTAAAAAA 420
 TCTGCCTGTG GGCAGTTTTT TTACTAGGTC CCCTTAGTTC AATGGATATA ACAACTCCCT 480
 . H I Y C S G
 CCTAAGGAGT AATTGCTGGT TCGATTCCGG CAGGGGACAT ATTCATTGCA TGTAATAGC 540
 G L S Y N S T R N R C P V Y E N C T F L
 GGTTTAGAGC TATTTTGCCC CAAATTTCTC TGATTAAGTT TATCGTTCCT ATCTTTTGT 600
 P K S S N Q G L N R Q N L K D N R D K Q
 TCTTGTAATT GATGTGCGTA AACTTCTAAA GTGATATTTA AATTCTCGTG ATCTAAACT 660
 E Q L Q H A Y V E L T I N L N E H D L V
 TGAGAGATGG AAATTAGATA GCTTGCAAAT GTATGCCTGA GAGAGTGCAC TCGTACCTCG 720
 Q S I S I L Y S A F T H R L S H V R V E
 CGACCAGTTA TTTTTCGGAT AGTTTTATTG ACTGCATTAT TTGAAAGTTT GTCGAATAAT 780
 R G T I K R I T K N V A N N S L K D F L
 CTGTCGTTTT TATTTTTTGT AAATTCATGC AAAAAAATA ATGTATCATT GTCAATTGGT 840
 R D N K N K T F E H L F F L T D N D I P
 ATATTTCTGA TACTACTTTT GTTTTTTGT GGCAGGTATC TTTGGTTGAA ATGATAATCC 900
 I N R I S S K N K T P L Y R Q N F H Y D
 CAAGTTTAT TAATTGATAA ATATTTGTGA GTGTAATCAA TATCATTAAC TGTTAAACCT 960
 W T K N I S L Y K N T Y D I D N V T L G
 AACATTTCAG CGAAGCGCAT GCCAGTTTTA GCGATGAGGT ATAACGCTGC ATACGATTGA 1020
 L C E A F R M
 <-----|
 TGTGTGATT TTTCTTTACA AATTTTATC AAGCGTAAGT ATTCATTGGT TTCAAGAAAT 1080
 TTTATCTCTA TTTACGCCCC TTATTTTTTG CTTAACCTT AGTGAATAAA CAAAATTTT 1140
 TTTCTATATA TCCCTCGTGA ACAGCCATGG ATACGCAGGC TTTTACATGT ATGTTAAAC 1200
 GCTTTACTGT ATCTTGACA TGCGTTTGAC TATAATGATT TATGACTTGT TGATATTTAG 1260

TGGAAGTAAT ATTGCAAAGT AATATATTTT CTATTATATG TTTATACGAT ATTCGATATT 1320
CCCACCCGTT GTCGCGTTTA CGGAAATACG CCATTGATAT ACTCCACATT AGCTAAAGAA 1380
CAGGGTGTTT AAGGCTACCT TGATGGAAAA GGCTCTCTTA GAGATATTTG TAAATGGTAT 1440
GATATCTCAA GTCGCTCTGT TCTCCAAAAG TGGATAAAC GGTATACTAG TGGTGAAGAC 1500
TTGAAAGCCA CTAGTAGAGG ATATAGCCGT ATGAAACAAG GAAGGCAAGC CACATTTGAA 1560
GAACGTGTAG AGATTGTTAA CTACACCATT GCCCATGGGA AAGACTATCA AGCAGCTATT 1620
GAGAAGTTTG GTGTTTCCTA CCAACAAATT TATTCTTGGG TGCCTAAGCT TGAGAAGAAT 1680
GGCTCACAAG GTTTGGTTGA TAGACGTGTG AAAGGGTTGG AGAGTAGGCC TGATTTAACC 1740
GAGATTGAGC AACTTTAACT CAAGATTAAA CAATTGGAGG AACGTAATCG TCTCTTAGAA 1800
ATCGAGGTTA GTTTACTAAA AAAGTTAGAA GACATCAAAC GAGGAAACAG ACGGTAAGAC 1860
TAGGTAAGCA TTTAGCGGAG TTCCAAGTAA TCAAGAATTA TTACGATGAG GAATCTAATG 1920
TGCCTATTCA GGCCTTATGC CAACTCTTGA AGGGGTCTCG TTCAGGCTAT TACAAGTGGC 1980
TCAATCGTCA AAAAACAGAT TTTGAGACAA AAAATACAAA GCTAATGGCT AAAATCAAGG 2040
AACTTCGTAG ACTCTACAAT GGTATCTTAG GTTATCGCCG TATGACAACA TTTATTAATC 2100
GTCAACTTGG GACAACTTAA AACAAGAAAC GGATTCGTTG ATTGATGAAC ATTCTGGGGA 2160
TTAGTTCAGT CATTCGTCGT GTTAGCCATG CTTGTACAAA AGCTGGTGAC AGATTTTACG 2220
AAGAAAATAT TCTTAATCGT GAATTTACAG CCACAGCTCA TAACCAGAAA TGGTGCACAG 2280
ATGTCACCTA TCTTCAATAC GGTCTGGGAG CTAAAGCTTA TCTCAGTGCG ATTAAAGACC 2340
TGTATAACGG TTCTATTATC GCTTATGAGA TTAGTCACAA CAATGAAATC CACTTGTTAT 2400
GAAGACCATT AAAAAGGGGC TAGAGCTCAA TCCAGGAGCC ACACCTATCA TCCATAGCGA 2460
TTGAGGTAGT CAATATACTT CCAAAGAATA CCGTTATATC ATACAACAAG CTGGTCTGAC 2520
CTTATCCATG TCCCGGATTG GCAAATGTAT TGATAATGCA CCAACTGAAA GTTTCTTTGG 2580
GTTTTTCAAG ACTGAGTCTT ACCACCTTAA GAAATACAAC TCTTATGATG AGTTGGTCAA 2640
TGATGTGGCA CGTTATATCG AATTCTACAA CACACAACGT TATCAATCAA AATTAAACAA 2700
CCTGACTCCT CTAGAATTCA GGAATCAGGT TGCATAACTT ATCTTTTATT ATTTGACTGT 2760
CTACTTGACA GGGAGCCGTT CAGATTGCTT AACCTTTCTA AATTTGCTAA AATAGCTACA 2820
AGAAAACGAG CCATTTAATG CTTATTTCTT ATACTGTCTT GCCTCAGCT CTCCTCGACC 2880
AAAAATTGAG CGTGAGGCTT TTTGTTTCAT TAAACGATGA TATTTCCATA TTCATCAGTT 2940
TGTTTTCCGA GAGCCATCAA AGCTTCGATA AGGTCGATAA TTCCAGGAAT AAAGGTAATA 3000
CTAAAAATAA TATATAAAAA AACCTGGCCT ATTTTTCCTG CGTAAAATTT ATGCGCTCCA 3060
ATGCCGCCCA AAAGAACGTT AATAAAACAT AAATACTAT GTTAGCATAA GACTTTATTT 3120

TTACAACTGA ATTTTCATATA AATGGATTAG AGTAAGGGAT AAAAGAAATT AGCATAGCTC 3180
 TTTTGAAAAT AAAAAAATTA ATATAATATG GAAAAAATTT TATTTTCATAA ACGTTTCATA 3240
 AAAGGTATGT AATCTAGTAT TTAGGCAACA CTATTTTGTC ACTGGTGTCT AGTAACTTAT 3300
 AGATTGATAA TTTTACTAGT AAACGTAATT CTTCGCTTTA AGAGTTAAAT GTCTATTTAT 3360
 TGTAAGCTAA ATTGGGAGGT GAACTTATGT AAAATTAGAT AGGTACTGTC AAGTACGGGA 3420
 TGATTATTGA AACAGCCAGT ATGCATCATA AAATCTGTAT TGCTTAATAA CTATTTTCCTT 3480
 AACCAGACAT CAGTTCATTG TTTATCATCG CTACCCTAAG TCTAGTTTTT TCAATAGAGC 3540
 ATTAGGTAGT TTTTGATAAT AAACTATAT AACATGAGA ATTAGATTTC GTATTGCATT 3600
 CTTCATAATG AGTTATTTGA GATTTTCCTT TGAATAAATA GATACGAAAT TCAGTAACTT 3660
 CATATATAAA CGGCTCTATC ATTGAGATAG TTTGTCAAAT GAAGAAATTT TTAATGGAAA 3720
 TAGTTTTTAA AACATTAGTT GTAGGCGATG TAAAAATATT AATCCAGTGG ATGCAATAGT 3780
 TGCGGAGTAA AAATAGAGAG GAGTAATTAG GAAGTGATAA AAAATGCTAT AGCATATATT 3840
 ACCAGAAAAA AAAATAGAAC ACTTATTATA TTTGCTATTT TAACAATTGT TCTTTCTTGC 3900
 TTGTATTCAT GTTTAACAAT AATGAAATCA AGTAATGAAA TAGAAAAGGC TTTATATGAA 3960
 M K S S N E I E K A L Y E
 |---->
 AGTTCTAATT CTTCAATATC AATTACAAAA AAAGATGGTA AATATTTTAA TATTAATCAA 4020
 S S N S S I S I T K K D G K Y F N I N Q
 TTTAAGAATA TTGAAAAAAT AAAAGAGGTT GAAGAAAAAA TATTTCAATA TGATGGATTA 4080
 F K N I E K I K E V E E K I F Q Y D G L
 GCAAAATTGA AAGATCTTAA AGTAGTTAGT GGTGAGCAAA GTATAAATAG AGAAGATTTA 4140
 A K L K D L K V V S G E Q S I N R E D L
 TCTGACGAAT TTAAAAATGT TGTTTCACTA GAAGCTACAA GTAATACTAA AAGAAATCTT 4200
 S D E F K N V V S L E A T S N T K R N L
 TTATTTAGTA GTGGAGTATT TAGTTTTTAA GAAGGAAAAA ATATAGAAGA AAATGATAAG 4260
 L F S S G V F S F K E G K N I E E N D K
 AATTCATTC TTGTTTCATGA AGAATTTGCT AAACAAAACA AACTAAAATT GGGTGATGAA 4320
 N S I L V H E E F A K Q N K L K L G D E
 ATTGATCTTG AATTACTAGA TACGGAAAAA AGTGGAAGAA TAAAAAGTCA TAAATTTAAA 4380
 I D L E L L D T E K S G K I K S H K F K
 ATTATAGGAA TCTTTTCTGG TAAAAACAG GAAACATATA CAGGATTATC ATCTGATTTT 4440
 I I G I F S G K K Q E T Y T G L S S D F
 AGCGAAAATA TGGTTTTTGT AGATTATTCA ACTAGCCAAG AAATATTAAA TAAATCAGAG 4500
 S E N M V F V D Y S T S Q E I L N K S E
 AATAATAGAA TTGCAAATAA AATTTTAATG TATTCTGGTA GTTTAGAATC TACAGAGCTT 4560
 N N R I A N K I L M Y S G S L E S T E L
 GCCTTAAACA AATTGAAAGA CTTTAAAATT GATAAGTCAA AGTATTCTAT TAAGAAAGAT 4620

A L N K L K D F K I D K S K Y S I K K D
AATAAGCAT TCGAAGAGTC TTTAGAGTCA GTGAGTGGAA TAAAACATAT AATTAAAATA 4680
N K A F E E S L E S V S G I K H I I K I
ATGACTTATT CGATTATGTT AGGTGGAATA GTTGTCTTT CATTAATCTT GATTCTATGG 4740
M T Y S I M L G G I V V L S L I L I L W
TTAAGAGAAA GAATTTATGA AATAGGTATA TTTTATCTA TTGGAACAAC TAAGATACAA 4800
L R E R I Y E I G I F L S I G T T K I Q
ATTATAAGGC AATTTATATT TGAGTTAATA TTCATATCAA TACCAAGTAT AATATCCTCC 4860
I I R Q F I F E L I F I S I P S I I S S
TTATTTTATAG GGAATCTACT ATTAAGAGTA ATTGTAGAAG GATTATTAA CTCAGAGAAC 4920
L F L G N L L L K V I V E G F I N S E N
TCAATGATTT TCGGTGGAAG TTTAATAAAT AAAAGCAGTT TTATGTTAAA CATAACAACA 4980
S M I F G G S L I N K S S F M L N I T T
CTTGCAGAAA GTTATTTAAT ATTAATAAGT ATTATTGTTT TATCAGTTGT AATGGCCTCT 5040
L A E S Y L I L I S I I V L S V V M A S
TCATTAATAT TATTTAAGAA ACCACAAGAA ATATTATCAA AAATAAGTTA GGAGCAAATA 5100
S L I L F K K P Q E I L S K I S .
ATGGATATAT TAGAAATAAA GAATGTAAAT TACAGTTACG CAAATTCTAA AGAAAAAGTT 5160
M D I L E I K N V N Y S Y A N S K E K V
|---->
TTGTCAGGAG TAAATCAAAA ATTTGAACTT GGAAAGTTTT ATGCGATAGT AGGGAAGTCA 5220
L S G V N Q K F E L G K F Y A I V G K S
GGAACAGGAA AATCCACACT TCTTTCCTTA CTTGCAGGAC TTGATAAAGT TCAAACAGGA 5280
G T G K S T L L S L L A G L D K V Q T G
AAAATCTTGT TTAAGAATGA AGATATAGAA AAGAAAGGAT ATAGTAATCA CAGAAAAAAT 5340
K I L F K N E D I E K K G Y S N H R K N
AATATATCTT TGGTATTTCA AAATTATAAT TTAATAGATT ATTTATCGCC GATTGAAAAT 5400
N I S L V F Q N Y N L I D Y L S P I E N
ATTAGACTAG TAAATAAATC AGTAGATGAG AGTATCTTGT TCGAATTAGG TTTAGATAAA 5460
I R L V N K S V D E S I L F E L G L D K
AAACAAATAA AAAGAAATGT TATGAAATTA TCTGGTGGTC AGCAACAAAG GGTAGCTATT 5520
K Q I K R N V M K L S G G Q Q Q R V A I
GCTAGGGCAC TGGTATCAGA TGCCCCAATA ATACTAGCTG ATGAGCCTAC CGGTAACCTA 5580
A R A L V S D A P I I L A D E P T G N L
GACAGTGTTA CTGCTGGAGA AATAATT (SEQ ID NO:27) 5607
D S V T A G E I I .

FIG. 5a

IQSLTEGQLR SDIPEFRAGD TVRVHAKVVE GTRERIQIFE GVVISRKGQG 50
ISEMYTVRKI SGGIGVERTF PIHTPRVDKI EVVRYGKVRR AKLYYLRALQ 100
GKAARIKEIR R (SEQ ID NO:28) 111

FIG. 5b

MRFAECLGLT VNDIDYTNKY LSINKTWDYH FNQRYLPTKN KSSIRNIPID 50
NDTLFFLHEF TKNKNDRLED KLSNNAVNKT IRKITGREVR VHSLRHTFAS 100
YLISISQVLD HENLNITLEV YAHQLQEQKD RNDKLNQRNL GQNSSKPLET 150
CNEYVPCNRN TSNYSLGGSC YIH (SEQ ID NO:29) 173

FIG. 5c

MKSSNEIEKA LYESSNSSIS ITKKDGKYFN INQFKNIEKI KEVEEKIFQY 50
DGLAKLKDLDK VVSGEQSINR EDLSDEFKNV VSLEATSNTK RNLLFSSGVF 100
SFKEGKNIEE NDKNSILVHE EFAKQNKLLK GDEIDLELLD TEKSGKIKSH 150
KFKIIGIFSG KKQETYTGSL SDFSENMFV DYSTSQEILN KSENNRIANK 200
ILMYSGSLES TELALNKLKD FKIDKSKYSI KKDKNKAFES LESVSGIKHI 250
IKIMTYSIML GGIVVLSLIL ILWLRERIYE IGIFLSIGTT KIQIIRQFIF 300
ELIFISIPSI ISSLFLGNLL LKVIVEGFN SENSMIFGGS LINKSSFMLN 350
ITTLAESYLI LISIIVLSVV MASSLILFKK PQEILSKIS 389
(SEQ ID NO:30)

FIG. 5d

MDILEIKNVN YSYANSKEKV LSGVNQKFEL GKFYAIVGKS GTGKSTLLSL 50
LAGLDKVQTG KILFKNEDIE KKGYSNHRKN NISLVFQNYN LIDYLSPIEN 100
IRLVNKSVDL SILFELGLDK KQIKRNVMKL SGGQQQRVAI ARALVSDAPI 150
ILADEPTGNL DSVTAGEII (SEQ ID NO:31) 169

FIG. 5e

CATATGACAA	TATTTTTC	AGTCTACATC	ACTTACTCGC	CTGTCGTGGA	AAATCTGGCA	60
ATACATTAAT	CGACCAATTA	GTTGCTGATG	GTTTACTTCA	TGCAGATAAT	CACTACCATT	120
TTTTCAATGG	GAAGTCTCTG	GCCACTTTCA	ATACTAACCA	ATTGATTTCG	GAAGTTGTCT	180
ATGTTGAAAT	ATCCTTAGAT	ACTATGTCTA	GTGGTGAACA	TGATTTAGTA	AAAGTTAACA	240
TTATCAGACC	CACTACCGAG	CATACTATCC	CCACGATGAT	GACAGCTAGC	CCCTATCATC	300
AAGGTATCAA	TGATCCTGCC	GCAGACCAAA	AAACATACCA	AATGGAGGGT	GCGCTAGCAG	360
TTAAACAGCC	TAAACACATA	CAAGTTGACA	CAAAACCATT	TAAAGAAGAA	GTAAACATC	420
CTTCAAAATT	ACCCATCAGC	CCTGCAACTG	AAAGCTTCAC	ACACATTGAC	AGTTATAGTC	480
TCAATGACTA	TTTTCTTTCT	CGTGGTTTTG	CTAATATATA	CGTTTCAGGT	GTGGGTACTG	540
CTGGCTCTAC	GGGTTTCATG	ACCAGTGGGG	ATTACCAACA	AATACAAAGC	TTTAAAGCAG	600
TCATTGATTG	GTTAAATGGT	AAGGTTACTG	CATTCACAAG	TCATAAACGA	GATAACAAG	660
TCAAGGCTGA	TTGGTCAAAC	GGCCTTGTAG	CAACCACAGG	TAAATCTTAT	CTCGGTACCA	720
TGTCAACTGG	TTTAGCAACA	ACTGGCGTTG	AGGGGCTGAA	AGTCATTATC	GCTGAAGCCG	780
CAATCTCCAC	ATGGTATGAT	TATTATCGAG	AAAATGGGCT	TGTGTGTAGT	CCAGGCGGCT	840
ACCCCGGTGA	AGATTTAGAC	GTTTTAACAG	AATTAACATA	CTCACGAAAC	CTCTTAGCTG	900
GTGATTACAT	CAAAAACAAC	GATTGCTATC	AAGCATTGTT	AAATGAACAA	TCAAAGCAA	960
TTGACCGTCA	AAGTGGGGAT	TACAACCAAT	ACTGGCATGA	CCGTAATTAC	CTAACTCACG	1020
TCAATAATGT	CAAAAGTCGA	GTAGTTTACA	CTCATGGACT	ACAGGATTGG	AATGTTAAGC	1080
CAAGACATGT	CTACAAAGTT	TTCAATGCAT	TGCCTCAAAC	CATCAAAAAA	CACCTTTTTT	1140
TACATCAAGG	TCAACATGTG	TATATGCATA	ATTGGCAGTC	GATTGATTTT	CGTGAAAGCA	1200
TGAATGCCTT	ACTAAGCCAA	GACTACTTIG	GCATTGACAA	TCATTTCCAA	TTAGAAGAGG	1260
TCATTTGGCA	AGATAATACT	ACTGAGCAAA	CTTGGCAAGT	TTTAGATGCT	TTCGGAGGAA	1320
ACCATCAAGA	GCAAATTGGT	TTAGGTGATA	GTAAAAAACT	TATTGATAAC	CATTATGACA	1380
AAGAAGCCTT	TGATACTTAT	TGTAAAGACT	TCAATGTGTT	CAAAAATGAT	CTTTTCAAGG	1440
GAAATAATAA	AACCAATCAA	ATCACTATTA	ATCTTCCTCT	AAAGAAAAAT	TATCTCCTGA	1500
ATGGACAGTG	CAAACTCCAT	CTACGTGTTA	AAACTAGTGA	CAAAAAGGCC	ATTTTATCAG	1560
CCCAAATCTT	AGACTATGGT	CCTAAAAAAC	GATTCAAAGA	TACACCAACC	ATCAAATTCT	1620
TAAACAGCCT	TGATAATGGT	AAAATTTTIG	CCAGAGAAGC	TTTACGTGAA	CTCCCGTTTA	1680
CTAAAGATCA	TTATCGTGTC	ATCAGTAAAG	GTGTCTTGAA	CCTTCAAAAT	CGTACAGACT	1740
TACTTACAAT	TGAGGCTATC	GAGCCAGAAC	AATGGTTTGA	TATCGAGTTT	AGCCTCCAAC	1800
CAAGTATATA	TCAATTGAGT	AAAGGTGATA	ATCTAAGGAT	TATCCTTTAT	ACAACTGATT	1860
TTGAACATAC	CATTCGAGAT	AATGCTAGTT	ACTCTATAAC	AGTAGATTTG	AGTCAATCTT	1920
ATTTAACTAT	CCCAACTAAT	CAAGGAAATT	AACTTATGAA	ACTTCTTACT	AAAGAACGGT	1980
TTGATGATTC	TCAACACTTT	TGGTACCAGA	TCAATTTATT	ACAAGAGAGT	AACTTCGGAG	2040
CAGTTTTTGA	CCATGATAAT	AAAAACATTC	CACAGGTTGT	TGCAACTATT	GTTGATGATT	2100
TACAAGGTTT	CGGAAGTTTC	AATCATTTCT	GGTATTTTGG	CAATACTACT	GATACTTCCA	2160
TCCTTATGAT	TGCTCATTTA	AATCGAAAAT	TCTATATTCA	GGTTAATTTA	AAGGACTTTG	2220
ACTTTGCACT	CAATTTAATA	GCTATAAATA	ATTGGAAGAG	TCTCCTCCAA	ACTCAACTTG	2280
AAGCTCTAAA	CGATACCCTA	GCAATATTTT	AATAAATAAG	GTAGAATGGA	GTGACAAAGC	2340
AACGCGAGGG	AGACTGATTA	ATGTCATCTT	ATTGGAATAA	CTATCCTGAA	CTTAAAAAAA	2400

ATATTGATGA AACCAATCAA CTAATTCAAG AAAGAATACA GGTCAGAAAT AAAGATATTG 2460
AAGCGGCGCT AAGCCAACTC ACAGCTGCGG GAGGAAAACA GCTCAGACCA GCATTCTTTT 2520
ACCTTTTTTC TCAACTTGGT AATAAGGAGA ATCAAGATAC TCAGCAACTA AAGAAAATCG 2580
CTGCTTCTTT AGAAATCCTT CACGTTGCTA CATTAATCCA TGATGATGTC ATTGATGACT 2640
CACCCTAAG ACGTGGAAT ATGACCATT CAAAGCAAGT TGGCAAAGAC ATCGCAGTTT 2700
ATACTGGGGA TTTACTTTTC ACAGTCTTTT TCGATCTTAT TTTAGAATCT ATGACTGATA 2760
CACCATTTAT GAGGATTAAT GCAAAATCTA TCGGTAAAT TCTCATGGGA GAATTGGACC 2820
AGATGCACCT TCGTTACAAT CAACAACAAG GTATCCATCA CTATTTACGT GCGATTTTCA 2880
GTAAGACAGC CGAACTCTTT AAATTAGCTA GCAAAGAAGG AGCTTACTTT GGTGGTGCAG 2940
AGAAGGAGGT TGTTTCTCTA GCAGGCCATA TCGGCTTTAA CATTGGTATG ACATTCCAAA 3000
TTTTGGATGA TATCCTGGAT TATACTGCAG ATAAAAAAC ATTTAATAAG CCTGTCTTAG 3060
AGGATTTAAC ACAAGGCGTT TACAGCCTT CTCTACTTCT TGCCATTGAA GAAAATCCTG 3120
ATATTTTCAA ACCTATTTTA GATAAAAAA CAGATATGGC TACTGAAGAC ATGGAAAAA 3180
TTGCTTATCT CGTCGTTTCC CATAGAGGTG TTGACAAAGC TCGCCATCTA GCTCGTAAAT 3240
TTACTGAGAA AGCTATTAGT GACATAAATA AGCTACCCCA GAACTCTGCA AAAAAACAGT 3300
TGCTACAATT AACTAATTAC CTTTTAAAAC GCAAATTTA AATAATAAAA AAACATTCCA 3360
CAATGCTAGA AAAGCAGTTA GGAATGTTT TTTTATTATC ATTTATTTAT CGCACCTATC 3420
AATCATCATA GATCACCATC ATCAGCGGCT TTCAGCTGAC GGTAACGTTG ACTACTTTGA 3480
GACAATTCTT GAGGAGAACC TTCCAACCT AATTGCCCAT TTTCTATAAA TAAGATACGA 3540
TCAGCATGTT CAATACCTTT TAAGTGATGT GTAATCCAAA CTAAGGTCTT ACCTTCCAAT 3600
TCTTTCATAA ATACCCTTAG TAAGGCTTGT TCAGTAATAG GATCAAGTCC AACAGTTGGC 3660
TCATCTAAGA TAACAATTGG GACATCTTTT AGTAAGATTC TAGCCAAAGC AATTCTATGC 3720
CTTTCGCCAC CTGAAAACCT AAGTCCAGCT TCATCAACCA TTGTATAGAG ACCATCTGAT 3780
AAATCAGTGA CCATCTCTTT CAATCCAAC CGTTCAAGAA CTTTCCATAC ATCTTCTTCA 3840
CTAGCATCTT GGTTTCCAAT GCGAATGTTA TTTAGCAGGG TTGTATTAAA AAGGTAGGGC 3900
GCTTGTTGTA TCACTCCAAT ATAGTTAGAA ATGCAATCAC CAACTATTGA AACATCAGCA 3960
CCGCCTAGGG TAATCTTCCC TTGACTTGCT TTCAAGTCGC CACGAAGTAG ACTAGCTAAG 4020
GTACTCTTGC CAGAACCACT CCGCCCTAAA ATAGCAATTT TTTCTCCTT TTTAATATCC 4080
AAATCTAAAT GATGCAAAAC CCATTTCTCT TGTGGCTTAT ACTGGAACT TAAATTCTTG 4140
ACGGAAAAAT CATATGGCTT ATTAGGCAAT T (SEQ ID NO:32) 4171

FIG. 6a

YDNIFQSLHH LLACRGKSGN TLIDQLVADG LLHADNHYHF FNGKSLATFN 50
 TNQLIREVVY VEISLDTMSS GEHDLVKVNI IRPTTEHTIP TMMTASPYHQ 100
 GINDPAADQK TYQMEGALAV KQPKHIQVDT KPFKEEVKHP SKLPISPATE 150
 SFTHIDSYSL NDYFLSRGFA NIYVSGVGTA GSTGFMTSGD YQQIQSFKAV 200
 IDWLNGKVTA FTSHKRDKQV KADWSNGLVA TTGKSYLGTM STGLATTGVE 250
 GLKVIIAEAA ISTWYDYRE NGLVCSPGGY PGEDLDVLTE LTYSRNLLAG 300
 DYIKNNDQYQ ALLNEQSKAI DRQSGDYNQY WHDRNYLTHV NNVKSRVVYT 350
 HGLQDWNVVP RHVYKVFNAL PQTIKKHLFL HQGQHVYMHN WQSIDFRESM 400
 NALLSQELLG IDNHFQLEEV IWQDNTTEQT WQVLDAFGGN HQEQIGLGDS 450
 KKLIDNHYDK EAFDQYCKDF NVFKNDLFKG NNKTNQITIN LPLKKNYLLN 500
 GQCKLHLRVK TSDKKAILSQ QILDYGPCKR FKDTPTIKFL NSLDNGKNFA 550
 REALRELFT KDHYRVISKG VLNQNRDLD LTIEAIEPEQ WFDIEFSLQP 600
 SIYQLSKGDN LRIILYTTDF EHTIRDNASY SITVDLSQSY LTIPTNQGN 649
 (SEQ ID NO:33)

FIG. 6b

MKLLTKERFD DSQHFQYQIN LLQESNFGAV FDHDNKNIPQ VVATIVDDLQ 50
 GSGSSNHFQY FGNTTDTSL MIAHLNRKFY IQVNLKDFDF ALNLIANNW 100
 KSLLOQTQLEA LNDTLAIFQ (SEQ ID NO:34) 119

FIG. 6c

MSSYWNNYPE LKKNIDETNQ LIQERIQVRN KDIEAALSQ TAAGGKQLRP 50
 AFFYLFSQLG NKENQDTQQL KKIAASLEIL HVATLIHDDV IDDSPLRRGN 100
 MTIQSKFGKD IAVYTGDLLE TVFFDLILES MTDTPFMRIN AKSMRKILMG 150
 ELDQMHLRYN QQQGIHHYLR AISGKTAELE KLASKEGAYF GGAEKEVVRL 200
 AGHIGFNIGM TFQILDDILD YTADKKTFNK PVLEDLTQGV YSLPLLLAIE 250
 ENPDIFKPIL DKKTDMATED MEKIAYLVVS HRGVDKARHL ARKFTEKAIS 300
 DINKLPQNSA KKQLLQLTNY LLKRKI (SEQ ID NO:35) 326

FIG. 6d

LPNKPYDFSV KNLSFQYKPQ EKWVLHHLDL DIKEGEKIAI LGRSGSGKST 50
LASLLRGDLK ASQGKITLGG ADVSIVGDCI SNYIGVIQQA PYLFNTTLLN 100
NIRIGNQDAS EEDVWKVLER VGLKEMVTDL SDGLYTMVDE AGLRFSGGER 150
HRIALARILL KDVPIVILDE PTVGLDPITE QALLRVFMKE LEGKTLVWIT 200
HHLKGIEHAD RILFIENGQL ELEGSPQELS QSSQRYRQLK AADDGDL 247
(SEQ ID NO:36)

FIG. 6e

AATTCTATTT	GGAGGTTTT	CTTGAATAAA	TGGTTAGTTA	AGGCAAGTTC	CTTAGTTGTT	60
TTAGGTGGTA	TGGTTTTATC	TGCGGGTTCC	CGAGTTTTAG	CGGATACTTA	TGTCCGTCCA	120
ATTGATAATG	GTAGAATTAC	AACAGGTTTC	AATGGTTATC	CTGGACATTG	TGGGGTGGAT	180
TATGCTGTTC	CGACTGGAAC	GATTATTAGG	GCAGTGGCAG	ATGGTACTGT	GAAATTTGCA	240
GGAGCTGGAG	CCAACTTTT	TTGGATGACA	GACTTAGCAG	GAAATTGTGT	CATGATTCAA	300
CATGCGGATG	GAATGCATAG	TGGTTACGCT	CATATGTCAC	GTGTGGTGGC	TAGGACTGGG	360
GAAAAAGTCA	AACAAGGAGA	TATCATCGGT	TACGTAGGAG	CAACTGGTAT	GGCGACGGGA	420
CCTCACCTTC	ATTTTGAATT	TTTACCAGCT	AACCCTAATT	TTCAAAATGG	TTTCCATGGA	480
CGTATCAATC	CAACGTCACT	AATTGCTAAC	GTTGCGACCT	TTAGTGGAAA	AACGCAAGCA	540
TCAGCTCCAA	GCATTAAGCC	ATTACAATCA	GCTCCTGTAC	AGAATCAATC	TAGTAAATTA	600
AAAGTGTATC	GAGTAGATGA	ATTACAAAAG	GTTAATGGTG	TTTGGTTAGT	CAAAAATAAC	660
ACCCTAACGC	CGACTGGGTT	TGATTGGAAC	GATAATGGTA	TACCAGCATC	AGAAATTGAT	720
GAGGTTGATG	CTAATGGTAA	TTTGACAGCT	GACCAGGTTT	TTCAAAAAGG	TGGTTACTTT	780
ATCTTTAATC	CTAAAACTCT	TAAGACTGTA	GAAAAACCCA	TCCAAGGAAC	AGCTGGTTTA	840
ACTTGGGCTA	AGACACGCTT	TGCTAATGGT	AGTTCAGTTT	GGCTTCGCGT	TGACAACAGT	900
CAAGAACTGC	TTTACAAATA	GTTTGAGGTA	TTGATTCATT	GTTTTAAATG	ACAGTTTGT	960
TACTAACTAA	GTACAATTTT	TTTAAACCGT	CTGAAAATAA	TTTTATAGTC	CAGTAAAGTG	1020
TGATATTATA	GTCTCGGACT	AATAAAAAGG	AAATAGGAAT	TGAAGCAATG	AAAATGAATA	1080
AAAAGGTACT	ATTGACATCG	ACAATGGCAG	CTTCGCTATT	ATCAGTCGCA	AGTGTTCAAG	1140
CACAAGAAAC	AGATACGACG	TGGACAGCAC	GTA CTGTTTC	AGAGGTAAAG	GCTGATTTGG	1200
TAAAGCAAGA	CAATAAATCA	TCATATACTG	TGAAATATGG	TGATACACTA	AGCGTTATTT	1260
CAGAAGCAAT	GTCAATTGAT	ATGAATGTCT	TAGCAAAAAT	TAATAACATT	GCAGATATCA	1320
ATCTTATTTA	TCCTGAGACA	ACACTGACAG	TAAC TTACGA	TCAGAAGAGT	CATACTGCCA	1380
CTTCAATGAA	AATAGAAACA	CCAGCAACAA	ATGCTGCTGG	TCAAACAACA	GCTACTGTGG	1440
ATTTGAAAAC	CAATCAAGTT	TCTGTTGCAG	ACCAAAAAGT	TTCTCTCAAT	ACAATTTCTG	1500
AAGGTATGAC	ACCAGAAGCA	GCAACAACGA	TTGTTTCGCC	AATGAAGACA	TATTC TTCTG	1560
CGCCAGCTTT	GAAATCAAAA	GAAGTATTAG	CACAAGAGCA	AGCTGTTAGT	CAAGCAGCAG	1620
CTAATGAACA	GGTATCAACA	GCTCCTGTGA	AGTCGATTAC	TTCAGAAGTT	CCAGCAGCTA	1680
AAGAGGAAGT	TAAACCAACT	CAGACGTCAG	TCAGTCAGTC	AACAACAGTA	TCACCAGCTT	1740
CTGTTGCCGC	TGAAACACCA	GCTCCAGTAG	CTAAAGTAGC	ACCGGTAAGA	ACTGTAGCAG	1800
CCCCTAGAGT	GGCAAGTGTT	AAAGTAGTCA	CTCCTAAAGT	AGAAACTGGT	GCATCACCAG	1860
AGCATGTATC	AGCTCCAGCA	GTTCTGTGA	CTACGACTTC	AACAGCTACA	GACAGTAAGT	1920
TACAAGCGAC	TGAAGTTAAG	AGCGTTCGGG	TAGCACAAAA	AGCTCCAACA	GCAACACCGG	1980
TAGCACAACC	AGCTTCAACA	ACAAATGCAG	TAGCTGCACA	TCCTGAAAAT	GCAGGGCTCC	2040
AACCTCATGT	TGCAGCTTAT	AAAGAAAAAG	TAGCGTCAAC	TTATGGAGTT	AATGAATTCA	2100
GTACATACCG	TGCAGGTGAT	CCAGGTGATC	ATGGTAAAGG	TTTAGCAGTC	GACTTTATTG	2160
TAGGTAAAAA	CCAAGCACTT	GGTAATGAAG	TTGCACAGTA	CTCTACACAA	AATATGGCAG	2220
CAAATAACAT	TTCATATGTT	ATCTGGCAAC	AAAAGTTTTA	CTCAAATACA	AATAGTATTT	2280
ATGGACCTGC	TAATACTTGG	AATGCAATGC	CAGATCGTGG	TGGCGTTACT	GCCAACCATT	2340
ATGACCATGT	TCACGTATCA	TTTAACAAAT	AATATAAAAA	AGGAAGCTAT	TTGGCTTCTT	2400

TTTTATATGC CTTGAATAGA CTTTCAAGGT TCTTATCTAA TTTTATTAA ATTGAGGAGA 2460
TTAAGCTATA AGTCTGAAAC TACTTTCACG TTAACCGTGA CTAAATCAAA ACGTTAAAC 2520
TAAAATCTAA GTCTGTAAAG ATTATTGAAA ACGCTTTAAA AACAGATATA ATAAGGTTTG 2580
TAGATATCTA AAATTAAAAA AGATAAGGAA GTGAGAATAT GCCACATCTA AGTAAAGAAG 2640
CTTTTAAAAA GCAAATAAAA AATGGCATT A TTGTGTCATG TCAAGCTTTG CCTGGGGAGC 2700
CTCTTTATAC TGAAAGTGGA GGTGTTATGC CTCTTTTAGC TTTGGCAGCT CAAGAAGCAG 2760
GAGCGGTTGG TATAAGAGCC AATAGTGTC GCGACATTAA GGAAATTCAA GAAGTTACTA 2820
ATTTACCTAT CATCGGCATT ATTAAACGTG AATATCCTCC ACAAGAACCA TTTATCACTG 2880
CTACGATGAC AGAGGTGGAT CAATTAGCTA GTTTAGATAT TGCAGTAATA GCCTTAGATT 2940
GTACACTTAG AGAGCGTCAT GATGGTTTGA GTGTAGCTGA GTTTATTCAA AAGATAAAAG 3000
GGAAATATCC TGAACAGTTG CTAATGGCTG ATATAAGTAC TTTTGAAGAA GGTAAAAATG 3060
CTTTTGAAGC AGGAGTTGAT TTTGTGGGTA CAACTCTATC TGGATACACA GATTACAGCC 3120
GCCAAGAAGA AGGACCGGAT ATAGAACTCC TTAATAAGCT TTGTCAAGCC GGTATAGATG 3180
TGATTGCGGA AGGTAAAATT CATACTCCTA AGCAAGCTAA TGAAATTAAT CATATAGGTG 3240
TTGCAGGAAT TGTAGTTGGT GGTGCTATCA CTAGACCAA AGAAATAGCG GAGCGTTTCA 3300
TCTCAGGACT TAGTTAAAAG TGTTACTCAA AAATCAAAT CAAAATAAAA AAGGGGAATA 3360
GTTATGAGTA TCAAAAAAAG TGTGATTGGT TTTTGCCTCG GAGCTGCAGC ATTATCAATG 3420
TTTGCTTGTG TAGACAGTAG TCAATCTGTT ATGGCTGCCG AGAAGGATAA AGTCGAAATT 3480
(SEQ ID NO:37)

FIG. 7a

NSIWRFFLNK WLVKASSLVV LGGMVLSAGS RVLADTYVRP IDNGRITTGF 50
NGYPGHCGVD YAVPTGTIIR AVADGTVKFA GAGANFSWMT DLAGNCVMIQ 100
HADGMHSGYA HMSRVVARTG EKVKQGDIIG YVGATGMATG PHLHFEFLPA 150
NPNFQNGFHG RINPTSLIAN VATFSGKTQA SAPSIKPLQS APVQNQSSKL 200
KVYRVDELQK VNGVWLKNN TLTPTGFDWN DNGIPASEID EVDANGNLTA 250
DQVLQKGGYF IFNPCTLKTV EKPIQGTAGL TWAKTRFANG SSVWLRVDNS 300
QELLYK (SEQ ID NO:38) 306

FIG. 7b

MKMNKKVLLT	STMAASLLSV	ASVQAQETDT	TWTARTVSEV	KADLVKQDNK	50
SSYTVKYGDT	LSVISEAMSI	DMNVLAKINN	IADINLIYPE	TTLTVTYDQK	100
SHTATSMKIE	TPATNAAGQT	TATVDLKTNQ	VSVADQKVSL	NTISEGMTPE	150
AATTIVSPMK	TYSSAPALKS	KEVLAQEQAV	SQAAANEQVS	TAPVKSITSE	200
VPAAKEEVKP	TQTSVSQSTT	VSPASVAAET	PAPVAKVAPV	RTVAAPRVAS	250
VKVVT PKVET	GASPEHVSAP	AVPVTTTSTA	TDSKLQATEV	KSVPVAQKAP	300
TATPVAQPAS	TTNAVAAHPE	NAGLQPHVAA	YKEKVASTYG	VNEFSTYRAG	350
DPGDHGKGLA	VDFIVGKNQA	LGNEVAQYST	QNMAANNISY	VIWQQKFYSN	400
TNSIYG PANT	WNAMPDRGGV	TANHYDHVHV	SFNK	(SEQ ID NO:39)	434

FIG. 7c

MPHLSKEAFK	KQIKNGIIVS	CQALPGEPLY	TESGGVMPLL	ALAAQEAGAV	50
GIRANSVRDI	KEIQEVTNLP	IIGIIKREYP	PQEPFITATM	TEVDQLASLD	100
IAVIALDCTL	RERHDGLSVA	EFIQIKIGKY	PEQLLMADIS	TFEEGKNAFE	150
AGVDFVGTTL	SGYTDYXRQE	EGPDIELLNK	LCQAGIDVIA	EGKIHTPKQA	200
NEINHIGVAG	IVVGGAITRP	KEIAERFISG	LS	(SEQ ID NO:40)	232

FIG. 7d

MSIKKSVIGF	CLGAAALSMF	ACVDSSQSVM	AAEKDKVEI	39
(SEQ ID NO:41)				

FIG. 7e

ATGAAAATGA	ATAAAAAGGT	ACTATTGACA	TCGACAATGG	CAGCTTCGCT	50
ATTATCAGTC	GCAAGTG TTC	AAGCACAAGA	AACAGATACG	ACGTGGACAG	100
CACGTACTGT	TTCAGAGGTA	AAGGCTGATT	TGGTAAAGCA	AGACAATAAA	150
TCATCATATA	CTGTGAAATA	TGGTGATACA	CTAAGCGTTA	TTTCAGAAGC	200
AATGTCAATT	GATATGAATG	TCTTAGCAAA	AATTAATAAC	ATTGCAGATA	250
TCAATCTTAT	TTATCCTGAG	ACAACACTGA	CAGTAACTTA	CGATCAGAAG	300
AGTCATACTG	CCACTTCAAT	GAAAATAGAA	ACACCAGCAA	CAAATGCTGC	350
TGGTCAAACA	ACAGCTACTG	TGGATTTGAA	AACCAATCAA	GTTTCTGTTG	400
CAGACCAAAA	AGTTTCTCTC	AATACAATTT	CGGAAGGTAT	GACACCAGAA	450
GCAGCAACAA	CGATTGTTTC	GCCAATGAAG	ACATATTCTT	CTGCGCCAGC	500
TTTGAAATCA	AAAGAAGTAT	TAGCACAAGA	GCAAGCTGTT	AGTCAAGCAG	550
CAGCTAATGA	ACAGGTATCA	ACAGCTCCTG	TGAAGTCGAT	TACTTCAGAA	600
GTTCCAGCAG	CTAAAGAGGA	AGTTAAACCA	ACTCAGACGT	CAGTCAGTCA	650
GTCAACAACA	GTATCACCAG	CTTCTGTTGC	CGCTGAAACA	CCAGCTCCAG	700
TAGCTAAAGT	AGCACCGGTA	AGAACTGTAG	CAGCCCCTAG	AGTGGCAAGT	750
GTTAAAGTAG	TCACTCCTAA	AGTAGAAACT	GGTGCATCAC	CAGAGCATGT	800
ATCAGCTCCA	GCAGTTCCTG	TGACTACGAC	TTCAACAGCT	ACAGACAGTA	850
AGTTACAAGC	GACTGAAGTT	AAGAGCGTTC	CGGTAGCACA	AAAAGCTCCA	900
ACAGCAACAC	CGGTAGCACA	ACCAGCTTCA	ACAACAAATG	CAGTAGCTGC	950
ACATCCTGAA	AATGCAGGGC	TCCAACCTCA	TGTTGCAGCT	TATAAAGAAA	1000
AAGTAGCGTC	AACTTATGGA	GTTAATGAAT	TCAGTACATA	CCGTGCAGGT	1050
GATCCAGGTG	ATCATGGTAA	AGGTTTAGCA	GTCGACTTTA	TTGTAGGTAA	1100
AAACCAAGCA	CTTGGTAATG	AAGTTGCACA	GTA CTCTACA	CAAAATATGG	1150
CAGCAAATAA	CATTTTCATAT	GTTATCTGGC	AACAAAAGTT	TTACTCAAAT	1200
ACAAATAGTA	TTTATGGACC	TGCTAATACT	TGGAATGCAA	TGCCAGATCG	1250
TGGTGGCGTT	ACTGCCAACC	ATTATGACCA	TGTTACAGTA	TCATTTAACA	1300
AATAA					1305

(SEQ ID NO:42)

FIG. 8

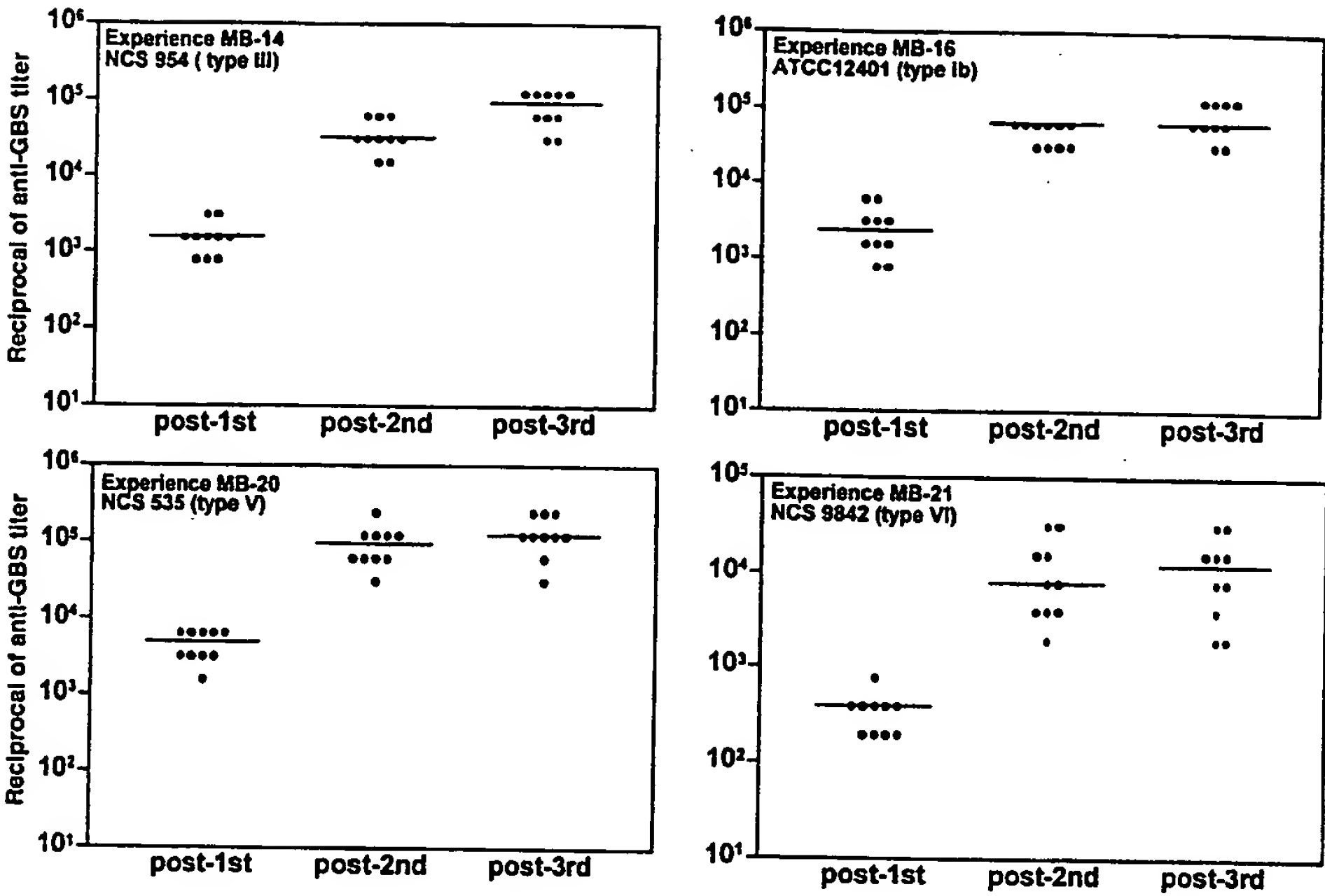
CAAGAAACAG	ATACGACGTG	GACAGCACGT	ACTGTTTCAG	AGGTAAAGGC	50
TGATTTGGTA	AAGCAAGACA	ATAAATCATC	ATATACTGTG	AAATATGGTG	100
ATACACTAAG	CGTTATTTCA	GAAGCAATGT	CAATTGATAT	GAATGTCTTA	150
GCAAAAATTA	ATAACATTGC	AGATATCAAT	CTTATTTATC	CTGAGACAAC	200
ACTGACAGTA	ACTTACGATC	AGAAGAGTCA	TACTGCCACT	TCAATGAAAA	250
TAGAAACACC	AGCAACAAAT	GCTGCTGGTC	AAACAACAGC	TACTGTGGAT	300
TTGAAAACCA	ATCAAGTTTC	TGTTGCAGAC	CAAAAAGTTT	CTCTCAATAC	350
AATTTTCGGAA	GGTATGACAC	CAGAAGCAGC	AACAACGATT	GTTTCGCCAA	400
TGAAGACATA	TTCTTCTGCG	CCAGCTTTGA	AATCAAAAGA	AGTATTAGCA	450
CAAGAGCAAG	CTGTTAGTCA	AGCAGCAGCT	AATGAACAGG	TATCAACAGC	500
TCCTGTGAAG	TCGATTACTT	CAGAAGTTCC	AGCAGCTAAA	GAGGAAGTTA	550
AACCAACTCA	GACGTCAGTC	AGTCAGTCAA	CAACAGTATC	ACCAGCTTCT	600
GTTGCCGCTG	AAACACCAGC	TCCAGTAGCT	AAAGTAGCAC	CGGTAAGAAC	650
TGTAGCAGCC	CCTAGAGTGG	CAAGTGTTAA	AGTAGTCACT	CCTAAAGTAG	700
AAACTGGTGC	ATCACCAGAG	CATGTATCAG	CTCCAGCAGT	TCCTGTGACT	750
ACGACTTCAA	CAGCTACAGA	CAGTAAGTTA	CAAGCGACTG	AAGTTAAGAG	800
CGTTCCGGTA	GCACAAAAAG	CTCCAACAGC	AACACCGGTA	GCACAACCAG	850
CTTCAACAAC	AAATGCAGTA	GCTGCACATC	CTGAAAATGC	AGGGCTCCAA	900
CCTCATGTTG	CAGCTTATAA	AGAAAAAGTA	GCGTCAACTT	ATGGAGTTAA	950
TGAATTCAGT	ACATACCGTG	CAGGTGATCC	AGGTGATCAT	GGTAAAGGTT	1000
TAGCAGTCGA	CTTTATTGTA	GGTAAAAACC	AAGCACTTGG	TAATGAAGTT	1050
GCACAGTACT	CTACACAAAA	TATGGCAGCA	AATAACATTT	CATATGTTAT	1100
CTGGCAACAA	AAGTTTTACT	CAAATACAAA	TAGTATTTAT	GGACCTGCTA	1150
ATACTTGGA	TGCAATGCCA	GATCGTGGTG	GCGTTACTGC	CAACCATTAT	1200
GACCATGTTC	ACGTATCATT	TAACAAATAA	(SEQ ID NO:43)		1230

FIG. 9

QETDTTWTAR	TVSEVKADLV	KQDNKSSYTV	KYGDTLSVIS	EAMSIDMNVL	50
AKINNIADIN	LIYPETTLTV	TYDQKSHTAT	SMKIETPATN	AAGQTTATVD	100
LKTNQVSVAD	QKVS LNTISE	GMTPEAATTI	VSPMKTYSSA	PALKSKEVLA	150
QEQAVSQAAA	NEQVSTAPVK	SITSEVPAAK	EEVKPTQTSV	SQSTTVSPAS	200
VAAETPAPVA	KVAPVRTVAA	PRVASVKVVT	PKVETGASPE	HVSAPAVPVT	250
TTSTATDSKL	QATEVKSVPV	AQKAPTATPV	AQPASTTNAV	AAHPENAGLQ	300
PHVAAYKEKV	ASTYGVNEFS	TYRAGDPGDH	GKGLAVDFIV	GKNQALGNEV	350
AQYSTQNMAA	NNISYVIWQQ	KFYSNTNSIY	GPANTWNAMP	DRGGVTANH Y	400
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FIG. 9a

Fig. 10



1 / 63

SEQUENCE LISTING

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 RIOUX, Clément
 DENIS, Martin
 BRODEUR, Bernard R.
 HAMEL, Josée
 CHARLEBOIS, Isabelle
 BOYER, Martine

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2/63

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3 / 63

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9/63

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10/63

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			405						410					415	
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			420					425					430		

11/63

Ala Gly Leu Leu Phe Pro Ile Arg Ala His Ile Thr Gly Gly Ser Ile
 435 440 445
 Glu Arg Leu His Tyr Ile Ile Ala Trp Glu Pro Ile Ala Leu Ala Thr
 450 455 460
 Leu Ile Leu Thr Leu Val Tyr Leu Cys Leu Val Lys Ile Leu Gln Gly
 465 470 475 480
 Lys Ser Cys Gln Ile Gly Asp Val Phe Asn Val Asp Arg Tyr Lys Lys
 485 490 495
 Leu Leu Gln Ala Tyr Gly Gly Ser Ser Asp Ser Gly Leu Ala Phe Leu
 500 505 510
 Asn Asp Lys Arg Leu Tyr Trp Tyr Gln Lys Asn Gly Glu Asp Cys Val
 515 520 525
 Ala Phe Gln Phe Val Ile Val Asn Asn Lys Cys Leu Ile Met Gly Glu
 530 535 540
 Pro Ala Gly Asp Asp Thr Tyr Ile Arg Glu Ala Ile Glu Ser Phe Ile
 545 550 555 560
 Asp Asp Ala Asp Lys Leu Asp Tyr Asp Leu Val Phe Tyr Ser Ile Gly
 565 570 575
 Gln Lys Leu Thr Leu Leu Leu His Glu Tyr Gly Phe Asp Phe Met Lys
 580 585 590
 Val Gly Glu Asp Ala Leu Val Asn Leu Glu Thr Phe Thr Leu Lys Gly
 595 600 605
 Asn Lys Tyr Lys Pro Phe Arg Asn Ala Leu Asn Arg Val Glu Lys Asp
 610 615 620
 Gly Phe Tyr Phe Glu Val Val Gln Ser Pro His Ser Gln Glu Leu Leu
 625 630 635 640
 Asn Ser Leu Glu Glu Ile Ser Asn Thr Trp Leu Glu Gly Arg Pro Glu
 645 650 655
 Lys Gly Phe Ser Leu Gly Tyr Phe Asn Lys Asp Tyr Phe Gln Gln Ala
 660 665 670
 Pro Ile Ala Leu Val Lys Asn Ala Glu His Glu Val Val Ala Phe Ala
 675 680 685
 Asn Ile Met Pro Asn Tyr Glu Lys Ser Ile Ile Ser Ile Asp Leu Met
 690 695 700
 Arg His Asp Lys Gln Lys Ile Pro Asn Gly Val Met Asp Phe Leu Phe
 705 710 715 720
 Leu Ser Leu Phe Ser Tyr Tyr Gln Glu Lys Gly Tyr His Tyr Phe Asp
 725 730 735
 Leu Gly Met Ala Pro Leu Ser Gly Val Gly Arg Val Glu Thr Ser Phe
 740 745 750
 Ala Lys Glu Arg Met Ala Tyr Leu Val Tyr His Phe Gly Ser His Phe
 755 760 765
 Tyr Ser Phe Asn Gly Leu His Lys Tyr Lys Lys Lys Phe Thr Pro Leu
 770 775 780
 Trp Ser Glu Arg Tyr Ile Ser Cys Ser Arg Ser Ser Trp Leu Ile Cys
 785 790 795 800
 Ala Ile Cys Ala Leu Leu Met Glu Asp Ser Lys Ile Lys Ile Val Lys
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<211> 518

<212> PRT

<213> Streptococcus

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12/63

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1				5					10					15	
Asn	Ile	Thr	Tyr	Ile	Met	Trp	Leu	Gln	Lys	Leu	Gly	Leu	Asp	Pro	Leu
			20					25					30		
Gln	Glu	Gln	Met	Leu	Trp	Gln	Phe	Pro	Gly	Leu	Leu	Leu	Gly	Val	Cys
		35					40					45			
Phe	Ile	Leu	Leu	Ala	Arg	Thr	Ile	Asp	Gln	Lys	Val	Lys	Asn	Ala	Phe
	50					55					60				
Pro	Ile	Ala	Ile	Ile	Trp	Ile	Thr	Leu	Thr	Leu	Phe	Tyr	Leu	Asn	Leu
65					70					75					80
Gly	His	Ile	Ser	Trp	Arg	Leu	Ser	Phe	Trp	Phe	Ile	Leu	Leu	Leu	Leu
				85					90					95	
Gly	Leu	Leu	Val	Ile	Lys	Pro	Thr	Leu	Tyr	Lys	Lys	Gln	Phe	Ile	Tyr
			100					105					110		
Ser	Trp	Glu	Glu	Arg	Ile	Lys	Asp	Gly	Ile	Ile	Ile	Val	Ser	Leu	Met
		115					120					125			
Gly	Val	Leu	Phe	Tyr	Ile	Ala	Gly	Leu	Leu	Phe	Pro	Ile	Arg	Ala	His
	130					135						140			
Ile	Thr	Gly	Gly	Ser	Ile	Glu	Arg	Leu	His	Tyr	Ile	Ile	Ala	Trp	Glu
145					150					155					160
Pro	Ile	Ala	Leu	Ala	Thr	Leu	Ile	Leu	Thr	Leu	Val	Tyr	Leu	Cys	Leu
				165					170					175	
Val	Lys	Ile	Leu	Gln	Gly	Lys	Ser	Cys	Gln	Ile	Gly	Asp	Val	Phe	Asn
			180					185					190		
Val	Asp	Arg	Tyr	Lys	Lys	Leu	Leu	Gln	Ala	Tyr	Gly	Gly	Ser	Ser	Asp
		195					200					205			
Ser	Gly	Leu	Ala	Phe	Leu	Asn	Asp	Lys	Arg	Leu	Tyr	Trp	Tyr	Gln	Lys
	210					215					220				
Asn	Gly	Glu	Asp	Cys	Val	Ala	Phe	Gln	Phe	Val	Ile	Val	Asn	Asn	Lys
225					230					235					240
Cys	Leu	Ile	Met	Gly	Glu	Pro	Ala	Gly	Asp	Asp	Thr	Tyr	Ile	Arg	Glu
				245					250					255	
Ala	Ile	Glu	Ser	Phe	Ile	Asp	Asp	Ala	Asp	Lys	Leu	Asp	Tyr	Asp	Leu
			260					265					270		
Val	Phe	Tyr	Ser	Ile	Gly	Gln	Lys	Leu	Thr	Leu	Leu	Leu	His	Glu	Tyr
		275					280					285			
Gly	Phe	Asp	Phe	Met	Lys	Val	Gly	Glu	Asp	Ala	Leu	Val	Asn	Leu	Glu
	290					295					300				
Thr	Phe	Thr	Leu	Lys	Gly	Asn	Lys	Tyr	Lys	Pro	Phe	Arg	Asn	Ala	Leu
305					310					315					320
Asn	Arg	Val	Glu	Lys	Asp	Gly	Phe	Tyr	Phe	Glu	Val	Val	Gln	Ser	Pro
				325					330					335	
His	Ser	Gln	Glu	Leu	Leu	Asn	Ser	Leu	Glu	Glu	Ile	Ser	Asn	Thr	Trp
			340					345					350		
Leu	Glu	Gly	Arg	Pro	Glu	Lys	Gly	Phe	Ser	Leu	Gly	Tyr	Phe	Asn	Lys
		355					360					365			
Asp	Tyr	Phe	Gln	Gln	Ala	Pro	Ile	Ala	Leu	Val	Lys	Asn	Ala	Glu	His
	370					375					380				
Glu	Val	Val	Ala	Phe	Ala	Asn	Ile	Met	Pro	Asn	Tyr	Glu	Lys	Ser	Ile
385					390					395					400
Ile	Ser	Ile	Asp	Leu	Met	Arg	His	Asp	Lys	Gln	Lys	Ile	Pro	Asn	Gly
				405					410					415	
Val	Met	Asp	Phe	Leu	Phe	Leu	Ser	Leu	Phe	Ser	Tyr	Tyr	Gln	Glu	Lys
		420						425				430			
Gly	Tyr	His	Tyr	Phe	Asp	Leu	Gly	Met	Ala	Pro	Leu	Ser	Gly	Val	Gly
		435					440					445			

13/63

Arg Val Glu Thr Ser Phe Ala Lys Glu Arg Met Ala Tyr Leu Val Tyr
 450 455 460
 His Phe Gly Ser His Phe Tyr Ser Phe Asn Gly Leu His Lys Tyr Lys
 465 470 475 480
 Lys Lys Phe Thr Pro Leu Trp Ser Glu Arg Tyr Ile Ser Cys Ser Arg
 485 490 495
 Ser Ser Trp Leu Ile Cys Ala Ile Cys Ala Leu Leu Met Glu Asp Ser
 500 505 510
 Lys Ile Lys Ile Val Lys
 515

<210> 7
 <211> 5126
 <212> DNA
 <213> Streptococcus

<220>
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<221> CDS
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 <222> (3106)...(4842)

<221> CDS
 <222> (4850)...(5125)

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Asn Phe Asp Ile Glu Thr Thr Thr Phe Glu Ala Met Lys Lys His Ala	
1 5 10 15	
tca tta ttg gag aaa ata tct gtt gag cgt tct ttt att gaa ttt gat	96
Ser Leu Leu Glu Lys Ile Ser Val Glu Arg Ser Phe Ile Glu Phe Asp	
20 25 30	
aaa ctt cta tta gca cct tat tgg cgt aaa gga atg ctg gca cta ata	144
Lys Leu Leu Leu Ala Pro Tyr Trp Arg Lys Gly Met Leu Ala Leu Ile	
35 40 45	
gat agt cat gct ttt aat tat cta cca tgc tta aaa aat agg gaa tta	192
Asp Ser His Ala Phe Asn Tyr Leu Pro Cys Leu Lys Asn Arg Glu Leu	
50 55 60	
caa tta agc gcc ttt ttg tcc cag tta gat aaa gat ttt tta ttt gag	240
Gln Leu Ser Ala Phe Leu Ser Gln Leu Asp Lys Asp Phe Leu Phe Glu	
65 70 75 80	
aca tca gaa caa gct tgg gca tca ctc atc ttg agt atg gaa gtt gaa	288
Thr Ser Glu Gln Ala Trp Ala Ser Leu Ile Leu Ser Met Glu Val Glu	
85 90 95	

14 / 63

cac aca aag act ttt tta aaa aaa tgg aag aca tca act cac ttt caa	336
His Thr Lys Thr Phe Leu Lys Lys Trp Lys Thr Ser Thr His Phe Gln	
100 105 110	
aaa gat gtt gag cat ata gtg gat gtt tat cgt att cgt gaa caa atg	384
Lys Asp Val Glu His Ile Val Asp Val Tyr Arg Ile Arg Glu Gln Met	
115 120 125	
gga ttg gct aaa gaa cat ctt tat cgt tat gga aaa act ata ata aaa	432
Gly Leu Ala Lys Glu His Leu Tyr Arg Tyr Gly Lys Thr Ile Ile Lys	
130 135 140	
caa gcg gaa ggt att cgc aaa gca aga ggc ttg atg gtt gat ttc gaa	480
Gln Ala Glu Gly Ile Arg Lys Ala Arg Gly Leu Met Val Asp Phe Glu	
145 150 155 160	
aaa ata gaa caa cta gat agt gag tta gca atc cat gat agg cat gag	528
Lys Ile Glu Gln Leu Asp Ser Glu Leu Ala Ile His Asp Arg His Glu	
165 170 175	
ata gtt gtc aat ggt ggc acc tta atc aag aaa tta gga ata aaa cct	576
Ile Val Val Asn Gly Gly Thr Leu Ile Lys Lys Leu Gly Ile Lys Pro	
180 185 190	
ggt cca cag atg gga gat att atc tct caa att gaa tta gcc att gtt	624
Gly Pro Gln Met Gly Asp Ile Ile Ser Gln Ile Glu Leu Ala Ile Val	
195 200 205	
tta gga caa ctg att aat gaa gaa gag gct att tta cat ttt gtt aag	672
Leu Gly Gln Leu Ile Asn Glu Glu Glu Ala Ile Leu His Phe Val Lys	
210 215 220	
cag tac ttg atg gat tagagaggat tat atg agc gat ttt tta gta gat	721
Gln Tyr Leu Met Asp Met Ser Asp Phe Leu Val Asp	
225 230 235	
gga ttg act aag tcg gtt ggt gat aag acg gtc ttt agt aat gtt tca	769
Gly Leu Thr Lys Ser Val Gly Asp Lys Thr Val Phe Ser Asn Val Ser	
240 245 250	
ttt atc atc cat agt tta gac cgt att ggg att att ggt gtc aat gga	817
Phe Ile Ile His Ser Leu Asp Arg Ile Gly Ile Ile Gly Val Asn Gly	
255 260 265	
act gga aag aca aca cta tta gat gtt att tcg ggt gaa tta ggt ttt	865
Thr Gly Lys Thr Thr Leu Leu Asp Val Ile Ser Gly Glu Leu Gly Phe	
270 275 280	
gat ggt gat cgt tcc cct ttt tca tca gct aat gat tat aag att gct	913
Asp Gly Asp Arg Ser Pro Phe Ser Ser Ala Asn Asp Tyr Lys Ile Ala	
285 290 295 300	
tat tta aaa caa gaa cca gac ttt gat gat tct cag aca att ttg gac	961
Tyr Leu Lys Gln Glu Pro Asp Phe Asp Asp Ser Gln Thr Ile Leu Asp	
305 310 315	

15/63

acc gta ctt tct tct gac tta aga gag atg gct tta att aaa gaa tat	1009
Thr Val Leu Ser Ser Asp Leu Arg Glu Met Ala Leu Ile Lys Glu Tyr	
320 325 330	
gaa tta ttg ctt aat cac tac gaa gaa agt aag caa tca cgt cta gag	1057
Glu Leu Leu Leu Asn His Tyr Glu Glu Ser Lys Gln Ser Arg Leu Glu	
335 340 345	
aaa gta atg gca gaa atg gat tct tta gat gct tgg tct att gag agc	1105
Lys Val Met Ala Glu Met Asp Ser Leu Asp Ala Trp Ser Ile Glu Ser	
350 355 360	
gaa gtc aaa aca gta tta tcc aaa tta ggt att act gat ttg cag ttg	1153
Glu Val Lys Thr Val Leu Ser Lys Leu Gly Ile Thr Asp Leu Gln Leu	
365 370 375 380	
tcg gtt ggt gaa tta tca gga gga tta cga aga cgt gtt caa tta gcg	1201
Ser Val Gly Glu Leu Ser Gly Gly Leu Arg Arg Arg Val Gln Leu Ala	
385 390 395	
caa gta tta tta aat gat gca gat tta ttg ctc tta gac gaa cct act	1249
Gln Val Leu Leu Asn Asp Ala Asp Leu Leu Leu Leu Asp Glu Pro Thr	
400 405 410	
aac cac tta gat att gac act att gca tgg tta acg aat ttt ttg aaa	1297
Asn His Leu Asp Ile Asp Thr Ile Ala Trp Leu Thr Asn Phe Leu Lys	
415 420 425	
aat agt aaa aag aca gtg ctt ttt ata act cat gat cgt tat ttt cta	1345
Asn Ser Lys Lys Thr Val Leu Phe Ile Thr His Asp Arg Tyr Phe Leu	
430 435 440	
gac aat gtt gca aca cgt att ttt gaa tta gat aag gca cag att aca	1393
Asp Asn Val Ala Thr Arg Ile Phe Glu Leu Asp Lys Ala Gln Ile Thr	
445 450 455 460	
gaa tat caa ggc aat tat cag gat tat gtc cga ctt cgt gca gaa caa	1441
Glu Tyr Gln Gly Asn Tyr Gln Asp Tyr Val Arg Leu Arg Ala Glu Gln	
465 470 475	
gac gag cgt gat gct gct agt tta cat aaa aag aaa cag ctt tat aaa	1489
Asp Glu Arg Asp Ala Ala Ser Leu His Lys Lys Lys Gln Leu Tyr Lys	
480 485 490	
cag gaa cta gct tgg atg cgt act cag cca caa gct cgt gca acg aaa	1537
Gln Glu Leu Ala Trp Met Arg Thr Gln Pro Gln Ala Arg Ala Thr Lys	
495 500 505	
caa cag gct cgt att aat cgt ttt caa aat cta aaa aac gat tta cac	1585
Gln Gln Ala Arg Ile Asn Arg Phe Gln Asn Leu Lys Asn Asp Leu His	
510 515 520	
caa aca agc gat aca agc gat ttg gaa atg aca ttt gaa aca agt cga	1633
Gln Thr Ser Asp Thr Ser Asp Leu Glu Met Thr Phe Glu Thr Ser Arg	
525 530 535 540	

16 / 63

att ggg aaa aag gtt att aat ttt gaa aat gtc tct ttt tct tac cca	1681
Ile Gly Lys Lys Val Ile Asn Phe Glu Asn Val Ser Phe Ser Tyr Pro	
545 550 555	
gat aaa tct atc ttg aaa gac ttt aat ttg tta att caa aat aaa gac	1729
Asp Lys Ser Ile Leu Lys Asp Phe Asn Leu Leu Ile Gln Asn Lys Asp	
560 565 570	
cgt att ggc atc gtt gga gat aat ggt gtt gga aag tca acc tta ctt	1777
Arg Ile Gly Ile Val Gly Asp Asn Gly Val Gly Lys Ser Thr Leu Leu	
575 580 585	
aat tta att gtt caa gat tta cag ccg gat tcg ggt aat gtc tct att	1825
Asn Leu Ile Val Gln Asp Leu Gln Pro Asp Ser Gly Asn Val Ser Ile	
590 595 600	
ggt gaa acg ata cgt gta ggt tac ttt tca caa caa ctt cat aat atg	1873
Gly Glu Thr Ile Arg Val Gly Tyr Phe Ser Gln Gln Leu His Asn Met	
605 610 615 620	
gat ggc tca aaa cgt gtt att aat tat ttg caa gag gtt gca gat gag	1921
Asp Gly Ser Lys Arg Val Ile Asn Tyr Leu Gln Glu Val Ala Asp Glu	
625 630 635	
gtt aaa act agt gtc ggt aca aca agt gtg aca gaa cta ttg gaa caa	1969
Val Lys Thr Ser Val Gly Thr Thr Ser Val Thr Glu Leu Leu Glu Gln	
640 645 650	
ttt ctc ttt cca cgt tcg aca cat gga aca caa att gca aaa tta tca	2017
Phe Leu Phe Pro Arg Ser Thr His Gly Thr Gln Ile Ala Lys Leu Ser	
655 660 665	
ggt ggt gag aaa aaa aga ctt tac ctt tta aaa atc ctg att gaa aag	2065
Gly Gly Glu Lys Lys Arg Leu Tyr Leu Leu Lys Ile Leu Ile Glu Lys	
670 675 680	
cct aat gtg tta cta ctt gat gag ccg aca aat gac tta gat att gct	2113
Pro Asn Val Leu Leu Leu Asp Glu Pro Thr Asn Asp Leu Asp Ile Ala	
685 690 695 700	
aca tta act gtt ctt gaa aat ttt tta caa ggc ttt ggt ggt cct gtg	2161
Thr Leu Thr Val Leu Glu Asn Phe Leu Gln Gly Phe Gly Gly Pro Val	
705 710 715	
att aca gtt agt cac gat cgt tac ttt tta gat aaa gtg gct aat aaa	2209
Ile Thr Val Ser His Asp Arg Tyr Phe Leu Asp Lys Val Ala Asn Lys	
720 725 730	
att att gcg ttt gaa gat aac gat atc cgt gaa ttt ttt ggt aat tat	2257
Ile Ile Ala Phe Glu Asp Asn Asp Ile Arg Glu Phe Phe Gly Asn Tyr	
735 740 745	
act gat tat tta gat gaa aaa gca ttt aat gag caa aat aat gaa gtt	2305
Thr Asp Tyr Leu Asp Glu Lys Ala Phe Asn Glu Gln Asn Asn Glu Val	
750 755 760	

17/63

atc agt aaa aaa gag agt acc aag aca agt cgt gaa aag caa agt cgt Ile Ser Lys Lys Glu Ser Thr Lys Thr Ser Arg Glu Lys Gln Ser Arg 765 770 775 780	2353
aaa aga atg tct tac ttt gaa aaa caa gaa tgg gcg aca att gaa gac Lys Arg Met Ser Tyr Phe Glu Lys Gln Glu Trp Ala Thr Ile Glu Asp 785 790 795	2401
gat att atg ata ttg gaa aat act atc act cgt ata gaa aat gat atg Asp Ile Met Ile Leu Glu Asn Thr Ile Thr Arg Ile Glu Asn Asp Met 800 805 810	2449
caa aca tgt ggt agt gat ttt aca agg tta tct gat tta caa aag gaa Gln Thr Cys Gly Ser Asp Phe Thr Arg Leu Ser Asp Leu Gln Lys Glu 815 820 825	2497
tta gat gca aaa aat gaa gca ctt cta gaa aag tat gac cgt tat gag Leu Asp Ala Lys Asn Glu Ala Leu Leu Glu Lys Tyr Asp Arg Tyr Glu 830 835 840	2545
tac ctt agt gag ttagacac atg att atc cgt ccg att att aaa aat gat Tyr Leu Ser Glu Leu Asp Thr Met Ile Ile Arg Pro Ile Ile Lys Asn Asp 845 850 855 860	2595
gac caa gca gtt gca caa tta att cga caa agt tta cgc gcc tat gat Asp Gln Ala Val Ala Gln Leu Ile Arg Gln Ser Leu Arg Ala Tyr Asp 865 870 875	2643
tta gat aaa cct gat aca gca tat tca gac cct cac tta gat cat ttg Leu Asp Lys Pro Asp Thr Ala Tyr Ser Asp Pro His Leu Asp His Leu 880 885 890	2691
acc tca tac tac gaa aaa ata gag aag tca gga ttc ttt gtc att gag Thr Ser Tyr Tyr Glu Lys Ile Glu Lys Ser Gly Phe Phe Val Ile Glu 895 900 905	2739
gag aga gat gag att att ggc tgt ggc ggc ttt ggt ccg ctg aaa aat Glu Arg Asp Glu Ile Ile Gly Cys Gly Gly Phe Gly Pro Leu Lys Asn 910 915 920 925	2787
cta att gca gag atg cag aag gtg tac att gca gaa cgt ttc cgt ggt Leu Ile Ala Glu Met Gln Lys Val Tyr Ile Ala Glu Arg Phe Arg Gly 930 935 940	2835
aag ggg ctt gct act gat tta gtg aaa atg att gaa gta gaa gct cga Lys Gly Leu Ala Thr Asp Leu Val Lys Met Ile Glu Val Glu Ala Arg 945 950 955	2883
aaa att ggg tat aga caa ctt tat tta gag aca gcc agt act ttg agt Lys Ile Gly Tyr Arg Gln Leu Tyr Leu Glu Thr Ala Ser Thr Leu Ser 960 965 970	2931
agg gca act gcg gtt tat aag cat atg gga tat tgt gcc tta tcg caa Arg Ala Thr Ala Val Tyr Lys His Met Gly Tyr Cys Ala Leu Ser Gln 975 980 985	2979

18/63

cca ata gca aat gat caa ggt cat aca gct atg gat att tgg atg att	3027
Pro Ile Ala Asn Asp Gln Gly His Thr Ala Met Asp Ile Trp Met Ile	
990 995 1000 1005	
aaa gat tta taagttgaaa gtggattagt gaacatggat taattatatt	3076
Lys Asp Leu	
gagataagag gaaagaaaag gagacatat atg gca tat att tgg tct tat ttg	3129
Met Ala Tyr Ile Trp Ser Tyr Leu	
1010 1015	
aaa agg tac ccc aat tgg tta tgg ctt gat tta cta gga gct atg ctt	3177
Lys Arg Tyr Pro Asn Trp Leu Trp Leu Asp Leu Leu Gly Ala Met Leu	
1020 1025 1030	
ttt gtg acg gtt atc cta gga atg ccc aca gcc tta gcg ggt atg att	3225
Phe Val Thr Val Ile Leu Gly Met Pro Thr Ala Leu Ala Gly Met Ile	
1035 1040 1045	
gat aat ggc gtt aca aaa ggt gat cgg act gga gtt tat ctg tgg acg	3273
Asp Asn Gly Val Thr Lys Gly Asp Arg Thr Gly Val Tyr Leu Trp Thr	
1050 1055 1060	
ttc atc atg ttt ata ttt gtt gta cta ggt att att ggg cgt att acg	3321
Phe Ile Met Phe Ile Phe Val Val Leu Gly Ile Ile Gly Arg Ile Thr	
1065 1070 1075 1080	
atg gct tac gca tct agt cgc tta acg aca aca atg att aga gat atg	3369
Met Ala Tyr Ala Ser Ser Arg Leu Thr Thr Thr Met Ile Arg Asp Met	
1085 1090 1095	
cgt aat gat atg tat gct aag ctt caa gaa tac tcc cat cat gaa tat	3417
Arg Asn Asp Met Tyr Ala Lys Leu Gln Glu Tyr Ser His His Glu Tyr	
1100 1105 1110	
gaa cag ata ggt gta tct tca cta gtg aca cgt atg aca agc gat act	3465
Glu Gln Ile Gly Val Ser Ser Leu Val Thr Arg Met Thr Ser Asp Thr	
1115 1120 1125	
ttt gtt ttg atg caa ttt gct gaa atg tct tta cgt tta ggc cta gta	3513
Phe Val Leu Met Gln Phe Ala Glu Met Ser Leu Arg Leu Gly Leu Val	
1130 1135 1140	
act cct atg gta atg att ttt agc gtg gtt atg ata cta att acg agt	3561
Thr Pro Met Val Met Ile Phe Ser Val Val Met Ile Leu Ile Thr Ser	
1145 1150 1155 1160	
cca tct ttg gct tgg ctt gta gcg gtt gcg atg cct ctt ttg gta gga	3609
Pro Ser Leu Ala Trp Leu Val Ala Val Ala Met Pro Leu Leu Val Gly	
1165 1170 1175	
gtc gtt tta tat gta gct ata aaa aca aaa cct tta tct gaa aga caa	3657
Val Val Leu Tyr Val Ala Ile Lys Thr Lys Pro Leu Ser Glu Arg Gln	
1180 1185 1190	

19/63

cag act atg ctt gat aaa atc aat caa tat gtt cgt gaa aat tta aca Gln Thr Met Leu Asp Lys Ile Asn Gln Tyr Val Arg Glu Asn Leu Thr 1195 1200 1205	3705
ggg tta cgc gtt gtt aga gcc ttt gca aga gag aat ttt caa tca caa Gly Leu Arg Val Val Arg Ala Phe Ala Arg Glu Asn Phe Gln Ser Gln 1210 1215 1220	3753
aaa ttt caa gtc gct aac caa cgt tac aca gat act tca act ggt ctt Lys Phe Gln Val Ala Asn Gln Arg Tyr Thr Asp Thr Ser Thr Gly Leu 1225 1230 1235 1240	3801
ttt aaa tta aca ggg cta aca gaa cca ctt ttc gtt caa att att att Phe Lys Leu Thr Gly Leu Thr Glu Pro Leu Phe Val Gln Ile Ile Ile 1245 1250 1255	3849
gca atg att gtg gct atc gtt tgg ttt gct ttg gat ccc tta caa aga Ala Met Ile Val Ala Ile Val Trp Phe Ala Leu Asp Pro Leu Gln Arg 1260 1265 1270	3897
ggt gct att aaa ata ggg gat tta gtt gct ttt atc gaa tat agc ttc Gly Ala Ile Lys Ile Gly Asp Leu Val Ala Phe Ile Glu Tyr Ser Phe 1275 1280 1285	3945
cat gct ctc ttt tca ttt ttg cta ttt gcc aat ctt ttt act atg tat His Ala Leu Phe Ser Phe Leu Leu Phe Ala Asn Leu Phe Thr Met Tyr 1290 1295 1300	3993
cct cgt atg gtg gta tca agc cat cgt att aga gag gtg atg gat atg Pro Arg Met Val Val Ser Ser His Arg Ile Arg Glu Val Met Asp Met 1305 1310 1315 1320	4041
cca atc tct atc aat cct aat gcc gaa ggt gtt acg gat acg aaa ctt Pro Ile Ser Ile Asn Pro Asn Ala Glu Gly Val Thr Asp Thr Lys Leu 1325 1330 1335	4089
aaa ggg cat tta gaa ttt gat aat gta aca ttc gct tat cca gga gaa Lys Gly His Leu Glu Phe Asp Asn Val Thr Phe Ala Tyr Pro Gly Glu 1340 1345 1350	4137
aca gag agt ccc gtt ttg cat gat att tct ttt aaa gct aag cct gga Thr Glu Ser Pro Val Leu His Asp Ile Ser Phe Lys Ala Lys Pro Gly 1355 1360 1365	4185
gaa aca att gct ttt att ggt tca aca ggt tca gga aaa tct tct ctt Glu Thr Ile Ala Phe Ile Gly Ser Thr Gly Ser Gly Lys Ser Ser Leu 1370 1375 1380	4233
gtt aat ttg att cca cgt ttt tat gat gtg aca ctt gga aaa atc tta Val Asn Leu Ile Pro Arg Phe Tyr Asp Val Thr Leu Gly Lys Ile Leu 1385 1390 1395 1400	4281
gta gat gga gtt gat gta aga gat tat aac ctt aaa tca ctt cgc caa Val Asp Gly Val Asp Val Arg Asp Tyr Asn Leu Lys Ser Leu Arg Gln 1405 1410 1415	4329

20 / 63

aag att gga ttt atc ccc caa aaa gct ctt tta ttt aca ggg aca ata Lys Ile Gly Phe Ile Pro Gln Lys Ala Leu Leu Phe Thr Gly Thr Ile 1420 1425 1430	4377
gga gag aat tta aaa tat gga aaa gct gat gct act att gat gat ctt Gly Glu Asn Leu Lys Tyr Gly Lys Ala Asp Ala Thr Ile Asp Asp Leu 1435 1440 1445	4425
aga caa gcg gtt gat att tct caa gct aaa gag ttt att gag agt cac Arg Gln Ala Val Asp Ile Ser Gln Ala Lys Glu Phe Ile Glu Ser His 1450 1455 1460	4473
caa gaa gcc ttt gaa acg cat tta gct gaa ggt ggg agc aat ctt tct Gln Glu Ala Phe Glu Thr His Leu Ala Glu Gly Gly Ser Asn Leu Ser 1465 1470 1475 1480	4521
ggg ggt caa aaa caa cgg tta tct att gct agg gct gtt gtt aaa gat Gly Gly Gln Lys Gln Arg Leu Ser Ile Ala Arg Ala Val Val Lys Asp 1485 1490 1495	4569
cca gat tta tat att ttt gat gat tca ttt tct gct ctc gat tat aag Pro Asp Leu Tyr Ile Phe Asp Asp Ser Phe Ser Ala Leu Asp Tyr Lys 1500 1505 1510	4617
aca gac gct act tta aga gcg cgt cta aaa gaa gta acc ggt gat tct Thr Asp Ala Thr Leu Arg Ala Arg Leu Lys Glu Val Thr Gly Asp Ser 1515 1520 1525	4665
aca gtt ttg ata gtt gct caa agg gtg ggt acg att atg gat gct gat Thr Val Leu Ile Val Ala Gln Arg Val Gly Thr Ile Met Asp Ala Asp 1530 1535 1540	4713
cag att att gtc ctt gat gaa ggc gaa att gtc ggt cgt ggt acc cac Gln Ile Ile Val Leu Asp Glu Gly Glu Ile Val Gly Arg Gly Thr His 1545 1550 1555 1560	4761
gct caa tta ata gaa aat aat gct att tat cgt gaa atc gct gag tca Ala Gln Leu Ile Glu Asn Asn Ala Ile Tyr Arg Glu Ile Ala Glu Ser 1565 1570 1575	4809
caa ctg aag aac caa aac tta tca gaa gga gag tgattgt atg aga aaa Gln Leu Lys Asn Gln Asn Leu Ser Glu Gly Glu Met Arg Lys 1580 1585 1590	4858
aaa tct gtt ttt ttg aga tta tgg tct tac cta act cgc tac aaa gct Lys Ser Val Phe Leu Arg Leu Trp Ser Tyr Leu Thr Arg Tyr Lys Ala 1595 1600 1605	4906
act ctt ttc tta gcg att ttt ttg aaa gtt tta tct agt ttt atg agt Thr Leu Phe Leu Ala Ile Phe Leu Lys Val Leu Ser Ser Phe Met Ser 1610 1615 1620	4954
ggt ctg gag cct ttt att tta ggg tta gcg ata aca gag ttg act gct Val Leu Glu Pro Phe Ile Leu Gly Leu Ala Ile Thr Glu Leu Thr Ala 1625 1630 1635	5002

21 / 63

aac ctt gtt gat atg gct aag gga gtt tct ggg gca gaa ttg aac gtt 5050
 Asn Leu Val Asp Met Ala Lys Gly Val Ser Gly Ala Glu Leu Asn Val
 1640 1645 1650
 cct tat att gct ggt att ttg att att tat ttt ttc aga ggt gtt ttc 5098
 Pro Tyr Ile Ala Gly Ile Leu Ile Ile Tyr Phe Phe Arg Gly Val Phe
 1655 1660 1665 1670
 tat gaa tta ggt tct tat ggc tca aat t 5126
 Tyr Glu Leu Gly Ser Tyr Gly Ser Asn
 1675

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 <211> 229
 <212> PRT
 <213> Streptococcus

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 Ser Leu Leu Glu Lys Ile Ser Val Glu Arg Ser Phe Ile Glu Phe Asp
 20 25 30
 Lys Leu Leu Leu Ala Pro Tyr Trp Arg Lys Gly Met Leu Ala Leu Ile
 35 40 45
 Asp Ser His Ala Phe Asn Tyr Leu Pro Cys Leu Lys Asn Arg Glu Leu
 50 55 60
 Gln Leu Ser Ala Phe Leu Ser Gln Leu Asp Lys Asp Phe Leu Phe Glu
 65 70 75 80
 Thr Ser Glu Gln Ala Trp Ala Ser Leu Ile Leu Ser Met Glu Val Glu
 85 90 95
 His Thr Lys Thr Phe Leu Lys Lys Trp Lys Thr Ser Thr His Phe Gln
 100 105 110
 Lys Asp Val Glu His Ile Val Asp Val Tyr Arg Ile Arg Glu Gln Met
 115 120 125
 Gly Leu Ala Lys Glu His Leu Tyr Arg Tyr Gly Lys Thr Ile Ile Lys
 130 135 140
 Gln Ala Glu Gly Ile Arg Lys Ala Arg Gly Leu Met Val Asp Phe Glu
 145 150 155 160
 Lys Ile Glu Gln Leu Asp Ser Glu Leu Ala Ile His Asp Arg His Glu
 165 170 175
 Ile Val Val Asn Gly Gly Thr Leu Ile Lys Lys Leu Gly Ile Lys Pro
 180 185 190
 Gly Pro Gln Met Gly Asp Ile Ile Ser Gln Ile Glu Leu Ala Ile Val
 195 200 205
 Leu Gly Gln Leu Ile Asn Glu Glu Glu Ala Ile Leu His Phe Val Lys
 210 215 220
 Gln Tyr Leu Met Asp
 225

<210> 9
 <211> 622
 <212> PRT
 <213> Streptococcus

22 / 63

<400> 9

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		20						25					30		
Gly	Ile	Ile	Gly	Val	Asn	Gly	Thr	Gly	Lys	Thr	Thr	Leu	Leu	Asp	Val
		35						40					45		
Ile	Ser	Gly	Glu	Leu	Gly	Phe	Asp	Gly	Asp	Arg	Ser	Pro	Phe	Ser	Ser
	50					55					60				
Ala	Asn	Asp	Tyr	Lys	Ile	Ala	Tyr	Leu	Lys	Gln	Glu	Pro	Asp	Phe	Asp
65					70					75					80
Asp	Ser	Gln	Thr	Ile	Leu	Asp	Thr	Val	Leu	Ser	Ser	Asp	Leu	Arg	Glu
			85					90						95	
Met	Ala	Leu	Ile	Lys	Glu	Tyr	Glu	Leu	Leu	Leu	Asn	His	Tyr	Glu	Glu
			100					105					110		
Ser	Lys	Gln	Ser	Arg	Leu	Glu	Lys	Val	Met	Ala	Glu	Met	Asp	Ser	Leu
		115						120					125		
Asp	Ala	Trp	Ser	Ile	Glu	Ser	Glu	Val	Lys	Thr	Val	Leu	Ser	Lys	Leu
		130					135					140			
Gly	Ile	Thr	Asp	Leu	Gln	Leu	Ser	Val	Gly	Glu	Leu	Ser	Gly	Gly	Leu
145					150					155					160
Arg	Arg	Arg	Val	Gln	Leu	Ala	Gln	Val	Leu	Leu	Asn	Asp	Ala	Asp	Leu
				165					170					175	
Leu	Leu	Leu	Asp	Glu	Pro	Thr	Asn	His	Leu	Asp	Ile	Asp	Thr	Ile	Ala
			180					185					190		
Trp	Leu	Thr	Asn	Phe	Leu	Lys	Asn	Ser	Lys	Lys	Thr	Val	Leu	Phe	Ile
		195						200					205		
Thr	His	Asp	Arg	Tyr	Phe	Leu	Asp	Asn	Val	Ala	Thr	Arg	Ile	Phe	Glu
	210					215						220			
Leu	Asp	Lys	Ala	Gln	Ile	Thr	Glu	Tyr	Gln	Gly	Asn	Tyr	Gln	Asp	Tyr
225					230					235					240
Val	Arg	Leu	Arg	Ala	Glu	Gln	Asp	Glu	Arg	Asp	Ala	Ala	Ser	Leu	His
				245					250					255	
Lys	Lys	Lys	Gln	Leu	Tyr	Lys	Gln	Glu	Leu	Ala	Trp	Met	Arg	Thr	Gln
			260					265					270		
Pro	Gln	Ala	Arg	Ala	Thr	Lys	Gln	Gln	Ala	Arg	Ile	Asn	Arg	Phe	Gln
		275						280					285		
Asn	Leu	Lys	Asn	Asp	Leu	His	Gln	Thr	Ser	Asp	Thr	Ser	Asp	Leu	Glu
	290					295					300				
Met	Thr	Phe	Glu	Thr	Ser	Arg	Ile	Gly	Lys	Lys	Val	Ile	Asn	Phe	Glu
305					310					315					320
Asn	Val	Ser	Phe	Ser	Tyr	Pro	Asp	Lys	Ser	Ile	Leu	Lys	Asp	Phe	Asn
				325					330					335	
Leu	Leu	Ile	Gln	Asn	Lys	Asp	Arg	Ile	Gly	Ile	Val	Gly	Asp	Asn	Gly
			340					345					350		
Val	Gly	Lys	Ser	Thr	Leu	Leu	Asn	Leu	Ile	Val	Gln	Asp	Leu	Gln	Pro
		355						360				365			
Asp	Ser	Gly	Asn	Val	Ser	Ile	Gly	Glu	Thr	Ile	Arg	Val	Gly	Tyr	Phe
	370					375					380				
Ser	Gln	Gln	Leu	His	Asn	Met	Asp	Gly	Ser	Lys	Arg	Val	Ile	Asn	Tyr
385					390					395					400
Leu	Gln	Glu	Val	Ala	Asp	Glu	Val	Lys	Thr	Ser	Val	Gly	Thr	Thr	Ser
				405					410					415	
Val	Thr	Glu	Leu	Leu	Glu	Gln	Phe	Leu	Phe	Pro	Arg	Ser	Thr	His	Gly
			420					425					430		

23 / 63

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Thr Gln Ile Ala Lys Leu Ser Gly Gly Glu Lys Lys Arg Leu Tyr Leu
      435                      440                      445
Leu Lys Ile Leu Ile Glu Lys Pro Asn Val Leu Leu Leu Asp Glu Pro
      450                      455                      460
Thr Asn Asp Leu Asp Ile Ala Thr Leu Thr Val Leu Glu Asn Phe Leu
465                      470                      475                      480
Gln Gly Phe Gly Gly Pro Val Ile Thr Val Ser His Asp Arg Tyr Phe
      485                      490                      495
Leu Asp Lys Val Ala Asn Lys Ile Ile Ala Phe Glu Asp Asn Asp Ile
      500                      505                      510
Arg Glu Phe Phe Gly Asn Tyr Thr Asp Tyr Leu Asp Glu Lys Ala Phe
      515                      520                      525
Asn Glu Gln Asn Asn Glu Val Ile Ser Lys Lys Glu Ser Thr Lys Thr
      530                      535                      540
Ser Arg Glu Lys Gln Ser Arg Lys Arg Met Ser Tyr Phe Glu Lys Gln
545                      550                      555                      560
Glu Trp Ala Thr Ile Glu Asp Asp Ile Met Ile Leu Glu Asn Thr Ile
      565                      570                      575
Thr Arg Ile Glu Asn Asp Met Gln Thr Cys Gly Ser Asp Phe Thr Arg
      580                      585                      590
Leu Ser Asp Leu Gln Lys Glu Leu Asp Ala Lys Asn Glu Ala Leu Leu
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Glu Lys Tyr Asp Arg Tyr Glu Tyr Leu Ser Glu Leu Asp Thr
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<210> 10
<211> 157
<212> PRT
<213> Streptococcus

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Ala Tyr Ser Asp Pro His Leu Asp His Leu Thr Ser Tyr Tyr Glu Lys
      35                      40                      45
Ile Glu Lys Ser Gly Phe Phe Val Ile Glu Glu Arg Asp Glu Ile Ile
      50                      55                      60
Gly Cys Gly Gly Phe Gly Pro Leu Lys Asn Leu Ile Ala Glu Met Gln
65                      70                      75                      80
Lys Val Tyr Ile Ala Glu Arg Phe Arg Gly Lys Gly Leu Ala Thr Asp
      85                      90                      95
Leu Val Lys Met Ile Glu Val Glu Ala Arg Lys Ile Gly Tyr Arg Gln
      100                      105                      110
Leu Tyr Leu Glu Thr Ala Ser Thr Leu Ser Arg Ala Thr Ala Val Tyr
      115                      120                      125
Lys His Met Gly Tyr Cys Ala Leu Ser Gln Pro Ile Ala Asn Asp Gln
      130                      135                      140
Gly His Thr Ala Met Asp Ile Trp Met Ile Lys Asp Leu
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<210> 11
<211> 579
<212> PRT
<213> Streptococcus

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24 / 63

<400> 11

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			20					25					30		
Pro	Thr	Ala	Leu	Ala	Gly	Met	Ile	Asp	Asn	Gly	Val	Thr	Lys	Gly	Asp
		35					40					45			
Arg	Thr	Gly	Val	Tyr	Leu	Trp	Thr	Phe	Ile	Met	Phe	Ile	Phe	Val	Val
	50					55				60					
Leu	Gly	Ile	Ile	Gly	Arg	Ile	Thr	Met	Ala	Tyr	Ala	Ser	Ser	Arg	Leu
65					70					75				80	
Thr	Thr	Thr	Met	Ile	Arg	Asp	Met	Arg	Asn	Asp	Met	Tyr	Ala	Lys	Leu
				85					90					95	
Gln	Glu	Tyr	Ser	His	His	Glu	Tyr	Glu	Gln	Ile	Gly	Val	Ser	Ser	Leu
			100					105					110		
Val	Thr	Arg	Met	Thr	Ser	Asp	Thr	Phe	Val	Leu	Met	Gln	Phe	Ala	Glu
	115					120						125			
Met	Ser	Leu	Arg	Leu	Gly	Leu	Val	Thr	Pro	Met	Val	Met	Ile	Phe	Ser
	130					135					140				
Val	Val	Met	Ile	Leu	Ile	Thr	Ser	Pro	Ser	Leu	Ala	Trp	Leu	Val	Ala
145					150					155					160
Val	Ala	Met	Pro	Leu	Leu	Val	Gly	Val	Val	Leu	Tyr	Val	Ala	Ile	Lys
				165					170					175	
Thr	Lys	Pro	Leu	Ser	Glu	Arg	Gln	Gln	Thr	Met	Leu	Asp	Lys	Ile	Asn
			180					185					190		
Gln	Tyr	Val	Arg	Glu	Asn	Leu	Thr	Gly	Leu	Arg	Val	Val	Arg	Ala	Phe
	195					200						205			
Ala	Arg	Glu	Asn	Phe	Gln	Ser	Gln	Lys	Phe	Gln	Val	Ala	Asn	Gln	Arg
	210					215					220				
Tyr	Thr	Asp	Thr	Ser	Thr	Gly	Leu	Phe	Lys	Leu	Thr	Gly	Leu	Thr	Glu
225					230					235					240
Pro	Leu	Phe	Val	Gln	Ile	Ile	Ile	Ala	Met	Ile	Val	Ala	Ile	Val	Trp
				245					250					255	
Phe	Ala	Leu	Asp	Pro	Leu	Gln	Arg	Gly	Ala	Ile	Lys	Ile	Gly	Asp	Leu
			260					265					270		
Val	Ala	Phe	Ile	Glu	Tyr	Ser	Phe	His	Ala	Leu	Phe	Ser	Phe	Leu	Leu
	275						280					285			
Phe	Ala	Asn	Leu	Phe	Thr	Met	Tyr	Pro	Arg	Met	Val	Val	Ser	Ser	His
	290					295					300				
Arg	Ile	Arg	Glu	Val	Met	Asp	Met	Pro	Ile	Ser	Ile	Asn	Pro	Asn	Ala
305					310					315					320
Glu	Gly	Val	Thr	Asp	Thr	Lys	Leu	Lys	Gly	His	Leu	Glu	Phe	Asp	Asn
				325					330					335	
Val	Thr	Phe	Ala	Tyr	Pro	Gly	Glu	Thr	Glu	Ser	Pro	Val	Leu	His	Asp
			340					345					350		
Ile	Ser	Phe	Lys	Ala	Lys	Pro	Gly	Glu	Thr	Ile	Ala	Phe	Ile	Gly	Ser
	355						360					365			
Thr	Gly	Ser	Gly	Lys	Ser	Ser	Leu	Val	Asn	Leu	Ile	Pro	Arg	Phe	Tyr
	370					375					380				
Asp	Val	Thr	Leu	Gly	Lys	Ile	Leu	Val	Asp	Gly	Val	Asp	Val	Arg	Asp
385					390					395					400
Tyr	Asn	Leu	Lys	Ser	Leu	Arg	Gln	Lys	Ile	Gly	Phe	Ile	Pro	Gln	Lys
				405					410					415	
Ala	Leu	Leu	Phe	Thr	Gly	Thr	Ile	Gly	Glu	Asn	Leu	Lys	Tyr	Gly	Lys
			420					425					430		

25 / 63

Ala Asp Ala Thr Ile Asp Asp Leu Arg Gln Ala Val Asp Ile Ser Gln
 435 440 445
 Ala Lys Glu Phe Ile Glu Ser His Gln Glu Ala Phe Glu Thr His Leu
 450 455 460
 Ala Glu Gly Gly Ser Asn Leu Ser Gly Gly Gln Lys Gln Arg Leu Ser
 465 470 475 480
 Ile Ala Arg Ala Val Val Lys Asp Pro Asp Leu Tyr Ile Phe Asp Asp
 485 490 495
 Ser Phe Ser Ala Leu Asp Tyr Lys Thr Asp Ala Thr Leu Arg Ala Arg
 500 505 510
 Leu Lys Glu Val Thr Gly Asp Ser Thr Val Leu Ile Val Ala Gln Arg
 515 520 525
 Val Gly Thr Ile Met Asp Ala Asp Gln Ile Ile Val Leu Asp Glu Gly
 530 535 540
 Glu Ile Val Gly Arg Gly Thr His Ala Gln Leu Ile Glu Asn Asn Ala
 545 550 555 560
 Ile Tyr Arg Glu Ile Ala Glu Ser Gln Leu Lys Asn Gln Asn Leu Ser
 565 570 575
 Glu Gly Glu

<210> 12
 <211> 92
 <212> PRT
 <213> Streptococcus

<400> 12
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 Tyr Lys Ala Thr Leu Phe Leu Ala Ile Phe Leu Lys Val Leu Ser Ser
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 Phe Met Ser Val Leu Glu Pro Phe Ile Leu Gly Leu Ala Ile Thr Glu
 35 40 45
 Leu Thr Ala Asn Leu Val Asp Met Ala Lys Gly Val Ser Gly Ala Glu
 50 55 60
 Leu Asn Val Pro Tyr Ile Ala Gly Ile Leu Ile Ile Tyr Phe Phe Arg
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 Gly Val Phe Tyr Glu Leu Gly Ser Tyr Gly Ser Asn
 85 90

<210> 13
 <211> 5215
 <212> DNA
 <213> Streptococcus

<220>
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26 / 63

<222> (2946)...(2716)
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 <223> of complementary strand

<221> CDS
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Phe Gly Ser Ala Leu Ser Thr Val Glu Val Lys Glu Ile Ile Ser	
1 5 10 15	
 gaa gaa aac ata tgg tta tat cgg ctc agt tgc tgc cat ttt act agc	95
Glu Glu Asn Ile Trp Leu Tyr Arg Leu Ser Cys Cys His Phe Thr Ser	
20 25 30	
 tac tca tat tgg aag tta cca act tgg taagcatcat atg ggt cta gca	144
Tyr Ser Tyr Trp Lys Leu Pro Thr Trp Met Gly Leu Ala	
35 40	
 aca aag gac aat cag att gcc tat att gat gac agc aaa ggt aag gca	192
Thr Lys Asp Asn Gln Ile Ala Tyr Ile Asp Asp Ser Lys Gly Lys Ala	
45 50 55 60	
 aaa gcc cct aaa aca aac aaa acg atg gat caa atc agt gct gaa gaa	240
Lys Ala Pro Lys Thr Asn Lys Thr Met Asp Gln Ile Ser Ala Glu Glu	
65 70 75	
 ggc atc tct gct gaa cag atc gta gtc aaa att act gac caa ggc tat	288
Gly Ile Ser Ala Glu Gln Ile Val Val Lys Ile Thr Asp Gln Gly Tyr	
80 85 90	
 gtg acc tca cac ggt gac cat tat cat ttt tac aat ggg aaa gtt cct	336
Val Thr Ser His Gly Asp His Tyr His Phe Tyr Asn Gly Lys Val Pro	
95 100 105	
 tat gat gcg att att agt gaa gag ttg ttg atg acg gat cct aat tac	384
Tyr Asp Ala Ile Ile Ser Glu Glu Leu Leu Met Thr Asp Pro Asn Tyr	
110 115 120	
 cgt ttt aaa caa tca gac gtt atc aat gaa atc tta gac ggt tac gtt	432
Arg Phe Lys Gln Ser Asp Val Ile Asn Glu Ile Leu Asp Gly Tyr Val	
125 130 135 140	

27/63

att aaa gtc aat ggc aac tat tat gtt tac ctc aag cca ggt agt aag	480
Ile Lys Val Asn Gly Asn Tyr Tyr Val Tyr Leu Lys Pro Gly Ser Lys	
145 150 155	
cgc aaa aac att cga acc aaa caa caa att gct gag caa gta gcc aaa	528
Arg Lys Asn Ile Arg Thr Lys Gln Gln Ile Ala Glu Gln Val Ala Lys	
160 165 170	
gga act aaa gaa gct aaa gaa aaa ggt tta gct caa gtg gcc cat ctc	576
Gly Thr Lys Glu Ala Lys Glu Lys Gly Leu Ala Gln Val Ala His Leu	
175 180 185	
agt aaa gaa gaa gtt gcg gca gtc aat gaa gca aaa aga caa gga cgc	624
Ser Lys Glu Glu Val Ala Ala Val Asn Glu Ala Lys Arg Gln Gly Arg	
190 195 200	
tat act aca gac gat ggc tat att ttt agt ccg aca gat atc att gat	672
Tyr Thr Thr Asp Asp Gly Tyr Ile Phe Ser Pro Thr Asp Ile Ile Asp	
205 210 215 220	
gat tta gga gat gct tat tta gta cct cat ggt aat cac tat cat tat	720
Asp Leu Gly Asp Ala Tyr Leu Val Pro His Gly Asn His Tyr His Tyr	
225 230 235	
att cct aaa aag gat ttg tct cca agt gag cta gct gct gca caa gcc	768
Ile Pro Lys Lys Asp Leu Ser Pro Ser Glu Leu Ala Ala Ala Gln Ala	
240 245 250	
tac tgg agt caa aaa caa ggt cga ggt gct aga ccg tct gat tac cgc	816
Tyr Trp Ser Gln Lys Gln Gly Arg Gly Ala Arg Pro Ser Asp Tyr Arg	
255 260 265	
ccg aca cca gcc cca ggt cgt agg aaa gcc cca att cct gat gtg acg	864
Pro Thr Pro Ala Pro Gly Arg Arg Lys Ala Pro Ile Pro Asp Val Thr	
270 275 280	
cct aac cct gga caa ggt cat cag cca gat aac ggt ggc tat cat cca	912
Pro Asn Pro Gly Gln Gly His Gln Pro Asp Asn Gly Gly Tyr His Pro	
285 290 295 300	
gcg cct cct agg cca aat gat gcg tca caa aac aaa cac caa aga gat	960
Ala Pro Pro Arg Pro Asn Asp Ala Ser Gln Asn Lys His Gln Arg Asp	
305 310 315	
gag ttt aaa gga aaa acc ttt aag gaa ctt tta gat caa cta cac cgt	1008
Glu Phe Lys Gly Lys Thr Phe Lys Glu Leu Leu Asp Gln Leu His Arg	
320 325 330	
ctt gat ttg aaa tac cgt cat gtg gaa gaa gat ggg ttg att ttt gaa	1056
Leu Asp Leu Lys Tyr Arg His Val Glu Glu Asp Gly Leu Ile Phe Glu	
335 340 345	
ccg act caa gtg atc aaa tca aac gct ttt ggg tat gtg gtg cct cat	1104
Pro Thr Gln Val Ile Lys Ser Asn Ala Phe Gly Tyr Val Val Pro His	
350 355 360	

28 / 63

gga gat cat tat cat att atc cca aga agt cag tta tca cct ctt gaa	1152
Gly Asp His Tyr His Ile Ile Pro Arg Ser Gln Leu Ser Pro Leu Glu	
365 370 375 380	
atg gaa tta gca gat cga tac tta gct ggc caa act gag gac aat gac	1200
Met Glu Leu Ala Asp Arg Tyr Leu Ala Gly Gln Thr Glu Asp Asn Asp	
385 390 395	
tca ggt tca gag cac tca aaa cca tca gat aaa gaa gtg aca cat acc	1248
Ser Gly Ser Glu His Ser Lys Pro Ser Asp Lys Glu Val Thr His Thr	
400 405 410	
ttt ctt ggt cat cgc atc aaa gct tac gga aaa ggc tta gat ggt aaa	1296
Phe Leu Gly His Arg Ile Lys Ala Tyr Gly Lys Gly Leu Asp Gly Lys	
415 420 425	
cca tat gat acg agt gat gct tat gtt ttt agt aaa gaa tcc att cat	1344
Pro Tyr Asp Thr Ser Asp Ala Tyr Val Phe Ser Lys Glu Ser Ile His	
430 435 440	
tca gtg gat aaa tca gga gtt aca gct aaa cac gga gat cat ttc cac	1392
Ser Val Asp Lys Ser Gly Val Thr Ala Lys His Gly Asp His Phe His	
445 450 455 460	
tat ata gga ttt gga gaa ctt gaa caa tat gag ttg gat gag gtc gct	1440
Tyr Ile Gly Phe Gly Glu Leu Glu Gln Tyr Glu Leu Asp Glu Val Ala	
465 470 475	
aac tgg gtg aaa gca aaa ggt caa gct gat gag ctt gct gct gct ttg	1488
Asn Trp Val Lys Ala Lys Gly Gln Ala Asp Glu Leu Ala Ala Ala Leu	
480 485 490	
gat cag gaa caa ggc aaa gaa aaa cca ctc ttt gac act aaa aaa gtg	1536
Asp Gln Glu Gln Gly Lys Glu Lys Pro Leu Phe Asp Thr Lys Lys Val	
495 500 505	
agt cgc aaa gta aca aaa gat ggt aaa gtg ggc tat atg atg cca aaa	1584
Ser Arg Lys Val Thr Lys Asp Gly Lys Val Gly Tyr Met Met Pro Lys	
510 515 520	
gat ggt aag gac tat ttc tat gct cgt gat caa ctt gat ttg act cag	1632
Asp Gly Lys Asp Tyr Phe Tyr Ala Arg Asp Gln Leu Asp Leu Thr Gln	
525 530 535 540	
att gcc ttt gcc gaa caa gaa cta atg ctt aaa gat aag aag cat tac	1680
Ile Ala Phe Ala Glu Gln Glu Leu Met Leu Lys Asp Lys Lys His Tyr	
545 550 555	
cgt tat gac att gtt gac aca ggt att gag cca cga ctt gct gta gat	1728
Arg Tyr Asp Ile Val Asp Thr Gly Ile Glu Pro Arg Leu Ala Val Asp	
560 565 570	
gtg tca agt ctg ccg atg cat gct ggt aat gct act tac gat act gga	1776
Val Ser Ser Leu Pro Met His Ala Gly Asn Ala Thr Tyr Asp Thr Gly	
575 580 585	

29/63

agt tcg ttt gtt atc cca cat att gat cat atc cat gtc gtt ccg tat	1824
Ser Ser Phe Val Ile Pro His Ile Asp His Ile His Val Val Pro Tyr	
590 595 600	
tca tgg ttg acg cgc gat cag att gca aca gtc aag tat gtg atg caa	1872
Ser Trp Leu Thr Arg Asp Gln Ile Ala Thr Val Lys Tyr Val Met Gln	
605 610 615 620	
cac ccc gaa gtt cgt ccg gat gta tgg tct aag cca ggg cat gaa gag	1920
His Pro Glu Val Arg Pro Asp Val Trp Ser Lys Pro Gly His Glu Glu	
625 630 635	
tca ggt tcg gtc att cca aat gtt acg cct ctt gat aaa cgt gct ggt	1968
Ser Gly Ser Val Ile Pro Asn Val Thr Pro Leu Asp Lys Arg Ala Gly	
640 645 650	
atg cca aac tgg caa att atc cat tct gct gaa gaa gtt caa aaa gcc	2016
Met Pro Asn Trp Gln Ile Ile His Ser Ala Glu Glu Val Gln Lys Ala	
655 660 665	
cta gca gaa ggt cgt ttt gca aca cca gac ggc tat att ttc gat cca	2064
Leu Ala Glu Gly Arg Phe Ala Thr Pro Asp Gly Tyr Ile Phe Asp Pro	
670 675 680	
cga gat gtt ttg gcc aaa gaa act ttt gta tgg aaa gat ggc tcc ttt	2112
Arg Asp Val Leu Ala Lys Glu Thr Phe Val Trp Lys Asp Gly Ser Phe	
685 690 695 700	
agc atc cca aga gca gat ggc agt tca ttg aga acc att aat aaa tct	2160
Ser Ile Pro Arg Ala Asp Gly Ser Ser Leu Arg Thr Ile Asn Lys Ser	
705 710 715	
gat cta tcc caa gct gag tgg caa caa gct caa gag tta ttg gca aag	2208
Asp Leu Ser Gln Ala Glu Trp Gln Gln Ala Gln Glu Leu Leu Ala Lys	
720 725 730	
aaa aat act ggt gat gct act gat acg gat aaa ccc aaa gaa aag caa	2256
Lys Asn Thr Gly Asp Ala Thr Asp Thr Asp Lys Pro Lys Glu Lys Gln	
735 740 745	
cag gca gat aag agc aat gaa aac caa cag cca agt gaa gcc agt aaa	2304
Gln Ala Asp Lys Ser Asn Glu Asn Gln Gln Pro Ser Glu Ala Ser Lys	
750 755 760	
gaa gaa aaa gaa tca gat gac ttt ata gac agt tta cca gac tat ggt	2352
Glu Glu Lys Glu Ser Asp Asp Phe Ile Asp Ser Leu Pro Asp Tyr Gly	
765 770 775 780	
cta gat aga gca acc cta gaa gat cat atc aat caa tta gca caa aaa	2400
Leu Asp Arg Ala Thr Leu Glu Asp His Ile Asn Gln Leu Ala Gln Lys	
785 790 795	
gct aat atc gat cct aag tat ctc att ttc caa cca gaa ggt gtc caa	2448
Ala Asn Ile Asp Pro Lys Tyr Leu Ile Phe Gln Pro Glu Gly Val Gln	
800 805 810	

31/63

<213> Streptococcus

<400> 14

Phe	Gly	Ser	Ala	Leu	Ser	Thr	Val	Glu	Val	Lys	Glu	Ile	Ile	Ser	Glu
1				5					10					15	
Glu	Asn	Ile	Trp	Leu	Tyr	Arg	Leu	Ser	Cys	Cys	His	Phe	Thr	Ser	Tyr
			20					25					30		
Ser	Tyr	Trp	Lys	Leu	Pro	Thr	Trp								
		35					40								

<210> 15

<211> 793

<212> PRT

<213> Streptococcus

<400> 15

Met	Gly	Leu	Ala	Thr	Lys	Asp	Asn	Gln	Ile	Ala	Tyr	Ile	Asp	Asp	Ser
1				5					10					15	
Lys	Gly	Lys	Ala	Lys	Ala	Pro	Lys	Thr	Asn	Lys	Thr	Met	Asp	Gln	Ile
			20					25					30		
Ser	Ala	Glu	Glu	Gly	Ile	Ser	Ala	Glu	Gln	Ile	Val	Val	Lys	Ile	Thr
		35					40					45			
Asp	Gln	Gly	Tyr	Val	Thr	Ser	His	Gly	Asp	His	Tyr	His	Phe	Tyr	Asn
	50					55					60				
Gly	Lys	Val	Pro	Tyr	Asp	Ala	Ile	Ile	Ser	Glu	Glu	Leu	Leu	Met	Thr
65					70					75				80	
Asp	Pro	Asn	Tyr	Arg	Phe	Lys	Gln	Ser	Asp	Val	Ile	Asn	Glu	Ile	Leu
			85					90					95		
Asp	Gly	Tyr	Val	Ile	Lys	Val	Asn	Gly	Asn	Tyr	Tyr	Val	Tyr	Leu	Lys
			100					105					110		
Pro	Gly	Ser	Lys	Arg	Lys	Asn	Ile	Arg	Thr	Lys	Gln	Gln	Ile	Ala	Glu
		115					120					125			
Gln	Val	Ala	Lys	Gly	Thr	Lys	Glu	Ala	Lys	Glu	Lys	Gly	Leu	Ala	Gln
	130					135					140				
Val	Ala	His	Leu	Ser	Lys	Glu	Glu	Val	Ala	Ala	Val	Asn	Glu	Ala	Lys
145					150					155				160	
Arg	Gln	Gly	Arg	Tyr	Thr	Thr	Asp	Asp	Gly	Tyr	Ile	Phe	Ser	Pro	Thr
			165					170						175	
Asp	Ile	Ile	Asp	Asp	Leu	Gly	Asp	Ala	Tyr	Leu	Val	Pro	His	Gly	Asn
			180					185					190		
His	Tyr	His	Tyr	Ile	Pro	Lys	Lys	Asp	Leu	Ser	Pro	Ser	Glu	Leu	Ala
	195					200						205			
Ala	Ala	Gln	Ala	Tyr	Trp	Ser	Gln	Lys	Gln	Gly	Arg	Gly	Ala	Arg	Pro
	210					215					220				
Ser	Asp	Tyr	Arg	Pro	Thr	Pro	Ala	Pro	Gly	Arg	Arg	Lys	Ala	Pro	Ile
225					230					235				240	
Pro	Asp	Val	Thr	Pro	Asn	Pro	Gly	Gln	Gly	His	Gln	Pro	Asp	Asn	Gly
			245					250					255		
Gly	Tyr	His	Pro	Ala	Pro	Pro	Arg	Pro	Asn	Asp	Ala	Ser	Gln	Asn	Lys
			260					265					270		
His	Gln	Arg	Asp	Glu	Phe	Lys	Gly	Lys	Thr	Phe	Lys	Glu	Leu	Leu	Asp
	275						280					285			
Gln	Leu	His	Arg	Leu	Asp	Leu	Lys	Tyr	Arg	His	Val	Glu	Glu	Asp	Gly
	290					295					300				
Leu	Ile	Phe	Glu	Pro	Thr	Gln	Val	Ile	Lys	Ser	Asn	Ala	Phe	Gly	Tyr
305					310					315					320

32 / 63

Val	Val	Pro	His	Gly	Asp	His	Tyr	His	Ile	Ile	Pro	Arg	Ser	Gln	Leu	325	330	335
Ser	Pro	Leu	Glu	Met	Glu	Leu	Ala	Asp	Arg	Tyr	Leu	Ala	Gly	Gln	Thr	340	345	350
Glu	Asp	Asn	Asp	Ser	Gly	Ser	Glu	His	Ser	Lys	Pro	Ser	Asp	Lys	Glu	355	360	365
Val	Thr	His	Thr	Phe	Leu	Gly	His	Arg	Ile	Lys	Ala	Tyr	Gly	Lys	Gly	370	375	380
Leu	Asp	Gly	Lys	Pro	Tyr	Asp	Thr	Ser	Asp	Ala	Tyr	Val	Phe	Ser	Lys	385	390	395
Glu	Ser	Ile	His	Ser	Val	Asp	Lys	Ser	Gly	Val	Thr	Ala	Lys	His	Gly	405	410	415
Asp	His	Phe	His	Tyr	Ile	Gly	Phe	Gly	Glu	Leu	Glu	Gln	Tyr	Glu	Leu	420	425	430
Asp	Glu	Val	Ala	Asn	Trp	Val	Lys	Ala	Lys	Gly	Gln	Ala	Asp	Glu	Leu	435	440	445
Ala	Ala	Ala	Leu	Asp	Gln	Glu	Gln	Gly	Lys	Glu	Lys	Pro	Leu	Phe	Asp	450	455	460
Thr	Lys	Lys	Val	Ser	Arg	Lys	Val	Thr	Lys	Asp	Gly	Lys	Val	Gly	Tyr	465	470	475
Met	Met	Pro	Lys	Asp	Gly	Lys	Asp	Tyr	Phe	Tyr	Ala	Arg	Asp	Gln	Leu	485	490	495
Asp	Leu	Thr	Gln	Ile	Ala	Phe	Ala	Glu	Gln	Glu	Leu	Met	Leu	Lys	Asp	500	505	510
Lys	Lys	His	Tyr	Arg	Tyr	Asp	Ile	Val	Asp	Thr	Gly	Ile	Glu	Pro	Arg	515	520	525
Leu	Ala	Val	Asp	Val	Ser	Ser	Phe	Val	Ile	Pro	His	Ala	Gly	Asn	Ala	530	535	540
Tyr	Asp	Thr	Gly	Ser	Ser	Phe	Val	Ile	Pro	His	Ile	Asp	His	Ile	His	545	550	555
Val	Val	Pro	Tyr	Ser	Trp	Leu	Thr	Arg	Asp	Gln	Ile	Ala	Thr	Val	Lys	565	570	575
Tyr	Val	Met	Gln	His	Pro	Glu	Val	Arg	Pro	Asp	Val	Trp	Ser	Lys	Pro	580	585	590
Gly	His	Glu	Glu	Ser	Gly	Ser	Val	Ile	Pro	Asn	Val	Thr	Pro	Leu	Asp	595	600	605
Lys	Arg	Ala	Gly	Met	Pro	Asn	Trp	Gln	Ile	Ile	His	Ser	Ala	Glu	Glu	610	615	620
Val	Gln	Lys	Ala	Leu	Ala	Glu	Gly	Arg	Phe	Ala	Thr	Pro	Asp	Gly	Tyr	625	630	635
Ile	Phe	Asp	Pro	Arg	Asp	Val	Leu	Ala	Lys	Glu	Thr	Phe	Val	Trp	Lys	645	650	655
Asp	Gly	Ser	Phe	Ser	Ile	Pro	Arg	Ala	Asp	Gly	Ser	Ser	Leu	Arg	Thr	660	665	670
Ile	Asn	Lys	Ser	Asp	Leu	Ser	Gln	Ala	Glu	Trp	Gln	Gln	Ala	Gln	Glu	675	680	685
Leu	Leu	Ala	Lys	Lys	Asn	Thr	Gly	Asp	Ala	Thr	Asp	Thr	Asp	Lys	Pro	690	695	700
Lys	Glu	Lys	Gln	Gln	Ala	Asp	Lys	Ser	Asn	Glu	Asn	Gln	Gln	Pro	Ser	705	710	715
Glu	Ala	Ser	Lys	Glu	Glu	Lys	Glu	Ser	Asp	Asp	Phe	Ile	Asp	Ser	Leu	725	730	735
Pro	Asp	Tyr	Gly	Leu	Asp	Arg	Ala	Thr	Leu	Glu	Asp	His	Ile	Asn	Gln	740	745	750
Leu	Ala	Gln	Lys	Ala	Asn	Ile	Asp	Pro	Lys	Tyr	Leu	Ile	Phe	Gln	Pro	755	760	765

33 / 63

Glu Gly Val Gln Phe Tyr Asn Lys Asn Gly Glu Leu Val Thr Tyr Asp
 770 775 780
 Ile Lys Thr Leu Gln Gln Ile Asn Pro
 785 790

<210> 16
 <211> 715
 <212> PRT
 <213> Streptococcus

<400> 16
 Met Thr Asp Pro Asn Tyr Arg Phe Lys Gln Ser Asp Val Ile Asn Glu
 1 5 10 15
 Ile Leu Asp Gly Tyr Val Ile Lys Val Asn Gly Asn Tyr Tyr Val Tyr
 20 25 30
 Leu Lys Pro Gly Ser Lys Arg Lys Asn Ile Arg Thr Lys Gln Gln Ile
 35 40 45
 Ala Glu Gln Val Ala Lys Gly Thr Lys Glu Ala Lys Glu Lys Gly Leu
 50 55 60
 Ala Gln Val Ala His Leu Ser Lys Glu Glu Val Ala Ala Val Asn Glu
 65 70 75 80
 Ala Lys Arg Gln Gly Arg Tyr Thr Thr Asp Asp Gly Tyr Ile Phe Ser
 85 90 95
 Pro Thr Asp Ile Ile Asp Asp Leu Gly Asp Ala Tyr Leu Val Pro His
 100 105 110
 Gly Asn His Tyr His Tyr Ile Pro Lys Lys Asp Leu Ser Pro Ser Glu
 115 120 125
 Leu Ala Ala Ala Gln Ala Tyr Trp Ser Gln Lys Gln Gly Arg Gly Ala
 130 135 140
 Arg Pro Ser Asp Tyr Arg Pro Thr Pro Ala Pro Gly Arg Arg Lys Ala
 145 150 155 160
 Pro Ile Pro Asp Val Thr Pro Asn Pro Gly Gln Gly His Gln Pro Asp
 165 170 175
 Asn Gly Gly Tyr His Pro Ala Pro Pro Arg Pro Asn Asp Ala Ser Gln
 180 185 190
 Asn Lys His Gln Arg Asp Glu Phe Lys Gly Lys Thr Phe Lys Glu Leu
 195 200 205
 Leu Asp Gln Leu His Arg Leu Asp Leu Lys Tyr Arg His Val Glu Glu
 210 215 220
 Asp Gly Leu Ile Phe Glu Pro Thr Gln Val Ile Lys Ser Asn Ala Phe
 225 230 235 240
 Gly Tyr Val Val Pro His Gly Asp His Tyr His Ile Ile Pro Arg Ser
 245 250 255
 Gln Leu Ser Pro Leu Glu Met Glu Leu Ala Asp Arg Tyr Leu Ala Gly
 260 265 270
 Gln Thr Glu Asp Asn Asp Ser Gly Ser Glu His Ser Lys Pro Ser Asp
 275 280 285
 Lys Glu Val Thr His Thr Phe Leu Gly His Arg Ile Lys Ala Tyr Gly
 290 295 300
 Lys Gly Leu Asp Gly Lys Pro Tyr Asp Thr Ser Asp Ala Tyr Val Phe
 305 310 315 320
 Ser Lys Glu Ser Ile His Ser Val Asp Lys Ser Gly Val Thr Ala Lys
 325 330 335
 His Gly Asp His Phe His Tyr Ile Gly Phe Gly Glu Leu Glu Gln Tyr
 340 345 350

34 / 63

Glu Leu Asp Glu Val Ala Asn Trp Val Lys Ala Lys Gly Gln Ala Asp
 355 360 365
 Glu Leu Ala Ala Ala Leu Asp Gln Glu Gln Gly Lys Glu Lys Pro Leu
 370 375 380
 Phe Asp Thr Lys Lys Val Ser Arg Lys Val Thr Lys Asp Gly Lys Val
 385 390 395 400
 Gly Tyr Met Met Pro Lys Asp Gly Lys Asp Tyr Phe Tyr Ala Arg Asp
 405 410 415
 Gln Leu Asp Leu Thr Gln Ile Ala Phe Ala Glu Gln Glu Leu Met Leu
 420 425 430
 Lys Asp Lys Lys His Tyr Arg Tyr Asp Ile Val Asp Thr Gly Ile Glu
 435 440 445
 Pro Arg Leu Ala Val Asp Val Ser Ser Leu Pro Met His Ala Gly Asn
 450 455 460
 Ala Thr Tyr Asp Thr Gly Ser Ser Phe Val Ile Pro His Ile Asp His
 465 470 475 480
 Ile His Val Val Pro Tyr Ser Trp Leu Thr Arg Asp Gln Ile Ala Thr
 485 490 495
 Val Lys Tyr Val Met Gln His Pro Glu Val Arg Pro Asp Val Trp Ser
 500 505 510
 Lys Pro Gly His Glu Glu Ser Gly Ser Val Ile Pro Asn Val Thr Pro
 515 520 525
 Leu Asp Lys Arg Ala Gly Met Pro Asn Trp Gln Ile Ile His Ser Ala
 530 535 540
 Glu Glu Val Gln Lys Ala Leu Ala Glu Gly Arg Phe Ala Thr Pro Asp
 545 550 555 560
 Gly Tyr Ile Phe Asp Pro Arg Asp Val Leu Ala Lys Glu Thr Phe Val
 565 570 575
 Trp Lys Asp Gly Ser Phe Ser Ile Pro Arg Ala Asp Gly Ser Ser Leu
 580 585 590
 Arg Thr Ile Asn Lys Ser Asp Leu Ser Gln Ala Glu Trp Gln Gln Ala
 595 600 605
 Gln Glu Leu Leu Ala Lys Lys Asn Thr Gly Asp Ala Thr Asp Thr Asp
 610 615 620
 Lys Pro Lys Glu Lys Gln Gln Ala Asp Lys Ser Asn Glu Asn Gln Gln
 625 630 635 640
 Pro Ser Glu Ala Ser Lys Glu Glu Lys Glu Ser Asp Asp Phe Ile Asp
 645 650 655
 Ser Leu Pro Asp Tyr Gly Leu Asp Arg Ala Thr Leu Glu Asp His Ile
 660 665 670
 Asn Gln Leu Ala Gln Lys Ala Asn Ile Asp Pro Lys Tyr Leu Ile Phe
 675 680 685
 Gln Pro Glu Gly Val Gln Phe Tyr Asn Lys Asn Gly Glu Leu Val Thr
 690 695 700
 Tyr Asp Ile Lys Thr Leu Gln Gln Ile Asn Pro
 705 710 715

<210> 17
 <211> 77
 <212> PRT
 <213> Streptococcus

<400> 17
 Met His Ser Phe Ser Asn Pro Gly Tyr Pro Tyr Asp Asn Ala Val Thr
 1 5 10 15

35 / 63

Glu Ala Phe Phe Lys Tyr Leu Lys His Arg Gln Ile Asn Arg Lys His
 20 25 30
 Tyr Gln Asn Ile Lys Gln Val Gln Leu Asp Cys Phe Glu Tyr Ile Glu
 35 40 45
 Asn Phe Tyr Asn Asn Tyr Asn Pro His Thr Ala Asn Leu Gly Leu Thr
 50 55 60
 Pro Asn Gln Lys Glu Glu Asn Tyr Phe Asn Ala Ile Lys
 65 70 75

<210> 18
 <211> 86
 <212> PRT
 <213> Streptococcus

<400> 18
 Met Ala Tyr Tyr Gln Ala Cys Thr Glu Lys Asp Ile Ile Arg Ser Met
 1 5 10 15
 Ser Arg Lys Gly Thr Pro Ala Asp Asn Ala Cys Ile Glu Trp Phe His
 20 25 30
 Thr Val Leu Lys Thr Glu Thr Phe Tyr Phe His Asn Arg Arg Lys Tyr
 35 40 45
 Asn Lys Asp Ser Ile Thr Asn Ile Val Lys Asn Tyr Ile Thr Phe Tyr
 50 55 60
 Asn Glu Thr Arg Ile Gln Gln Arg Leu Asn Asp Gln Ser Pro Val Gln
 65 70 75 80
 Tyr Arg Lys Leu Ile Ala
 85

<210> 19
 <211> 126
 <212> PRT
 <213> Streptococcus

<400> 19
 Met Glu Asn His Phe Ile Tyr Gly Tyr Arg Thr Ile Thr Arg Leu Leu
 1 5 10 15
 Lys Lys Ile His Gly Leu Thr Val Asn Thr Lys Lys Val Tyr Arg Ile
 20 25 30
 Met Lys Asn Asn Gly Trp Leu Cys Arg Thr Arg Thr Lys Lys Val Pro
 35 40 45
 Asn Leu Gly Lys Ala Tyr Tyr Leu Thr Asp Asn Lys Leu Ser Arg Asp
 50 55 60
 Phe His Ala Asp Lys Pro Lys Glu Lys Leu Val Thr Asp Ile Thr Tyr
 65 70 75 80
 Leu Tyr Phe Gly Asn Cys Lys Leu Tyr Leu Ser Ser Ile Met Asn Leu
 85 90 95
 Tyr Asn Arg Glu Ile Ile Ala Tyr Thr Ile Ser Asp Cys Gln Asp Thr
 100 105 110
 Asp Phe Val Leu Asp Thr Leu Asn Gln Leu Lys Leu Pro Lys
 115 120 125

<210> 20
 <211> 96
 <212> PRT
 <213> Streptococcus

36 / 63

<400> 20

Met	Val	Lys	Lys	Ala	Tyr	Ser	Trp	Glu	Thr	Lys	Leu	Ala	Cys	Ile	Asp
1				5					10					15	
Met	Lys	Lys	Ala	Gly	Lys	Ser	Asn	Arg	Val	Ile	Met	Glu	Thr	Leu	Gly
			20					25					30		
Ile	Lys	Asn	Asn	Ser	Gln	Ile	Tyr	Thr	Trp	Met	Lys	Trp	Tyr	Glu	Asn
		35					40					45			
Glu	Glu	Leu	Tyr	Arg	Phe	His	Gln	Gly	Val	Gly	Lys	Gln	Tyr	Thr	Tyr
	50					55					60				
Gly	Lys	Gly	Leu	Glu	His	Leu	Ser	Glu	Val	Glu	Gln	Leu	Gln	Leu	Gln
65					70					75					80
Val	Asp	Leu	Leu	Lys	Lys	Tyr	Arg	Gly	Leu	Ile	Arg	Lys	Ser	Ile	Lys
				85					90					95	

<210> 21

<211> 288

<212> PRT

<213> streptococcus

<400> 21

Ile	Arg	Tyr	Pro	Lys	Ala	Ser	Ser	Gly	Asp	Tyr	Gly	Thr	Lys	Arg	Glu
1				5					10					15	
Ile	Ile	Thr	Ala	Asn	Lys	Asp	Lys	Tyr	Ser	Ile	Ser	Lys	Met	Cys	Arg
			20					25					30		
Trp	Leu	Asn	Met	Pro	His	Ser	Ser	Tyr	Tyr	Tyr	Gln	Ala	Val	Glu	Ser
		35					40					45			
Val	Ser	Glu	Thr	Glu	Phe	Glu	Glu	Thr	Ile	Lys	Arg	Ile	Phe	Leu	Asp
	50					55					60				
Ser	Glu	Ser	Arg	Tyr	Gly	Ser	Arg	Lys	Ile	Lys	Ile	Cys	Leu	Asn	Asn
65					70				75						80
Glu	Gly	Ile	Thr	Leu	Ser	Arg	Arg	Arg	Ile	Arg	Arg	Ile	Met	Lys	Arg
				85					90					95	
Leu	Asn	Leu	Val	Ser	Val	Tyr	Gln	Lys	Ala	Thr	Phe	Lys	Pro	His	Ser
			100					105					110		
Arg	Gly	Lys	Asn	Glu	Ala	Pro	Ile	Pro	Asn	His	Leu	Asp	Arg	Gln	Phe
	115						120					125			
Lys	Gln	Glu	Arg	Pro	Leu	Gln	Ala	Leu	Val	Thr	Asp	Leu	Thr	Tyr	Val
	130					135					140				
Arg	Val	Gly	Asn	Arg	Trp	Ala	Tyr	Val	Cys	Leu	Ile	Ile	Asp	Leu	Tyr
145					150					155					160
Asn	Arg	Glu	Ile	Ile	Gly	Leu	Ser	Leu	Gly	Trp	His	Lys	Thr	Ala	Glu
				165					170					175	
Leu	Val	Lys	Gln	Ala	Ile	Gln	Ser	Ile	Pro	Tyr	Ala	Leu	Thr	Lys	Val
			180					185					190		
Lys	Met	Phe	His	Ser	Asp	Arg	Gly	Lys	Glu	Phe	Asp	Asn	Gln	Leu	Ile
	195						200					205			
Asp	Glu	Ile	Leu	Glu	Ala	Phe	Gly	Ile	Thr	Arg	Ser	Leu	Ser	Gln	Ala
	210					215					220				
Gly	Tyr	Pro	Tyr	Asp	Asn	Ala	Val	Ala	Glu	Ser	Thr	Tyr	Arg	Ala	Phe
225					230					235					240
Lys	Ile	Glu	Phe	Val	Tyr	Gln	Glu	Thr	Phe	Gln	Leu	Leu	Glu	Glu	Leu
			245						250					255	
Ala	Leu	Lys	Thr	Lys	Asp	Tyr	Val	His	Trp	Trp	Asn	Tyr	His	Arg	Ile
			260					265					270		
His	Gly	Ser	Leu	Asn	Tyr	Gln	Thr	Pro	Met	Thr	Lys	Arg	Leu	Ile	Ala
		275					280					285			

37 / 63

<210> 22
 <211> 5058
 <212> DNA
 <213> streptococcus

<220>
 <221> CDS
 <222> (1)...(663)

<221> CDS
 <222> (763)...(1344)

<221> CDS
 <222> (1362)...(1739)

<221> CDS
 <222> (2266)...(5058)

<400> 22

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Asn Leu Lys Ala Glu Leu Ser Val Glu Asp Glu Gln Tyr Thr Ala Thr	
1 5 10 15	
ggt tat ggt aaa tct gct cat ggt tca aca cca caa gaa ggt gtt aat	96
Val Tyr Gly Lys Ser Ala His Gly Ser Thr Pro Gln Glu Gly Val Asn	
20 25 30	
ggg gcg act tat tta gct ctt tat cta agt caa ttt gat ttt gaa ggt	144
Gly Ala Thr Tyr Leu Ala Leu Tyr Leu Ser Gln Phe Asp Phe Glu Gly	
35 40 45	
cct gct cgt gct ttc tta gat gtt aca gcc aac att att cac gaa gac	192
Pro Ala Arg Ala Phe Leu Asp Val Thr Ala Asn Ile Ile His Glu Asp	
50 55 60	
ttc tca ggt gaa aaa ctt gga gta gct tat gaa gat gac tgt atg gga	240
Phe Ser Gly Glu Lys Leu Gly Val Ala Tyr Glu Asp Asp Cys Met Gly	
65 70 75 80	
cca ttg agc atg aat gca ggt gtc ttc cag ttt gat gaa act aat gat	288
Pro Leu Ser Met Asn Ala Gly Val Phe Gln Phe Asp Glu Thr Asn Asp	
85 90 95	
gat aat act atc gct ctt aat ttc cgt tac cca caa ggg aca gat gct	336
Asp Asn Thr Ile Ala Leu Asn Phe Arg Tyr Pro Gln Gly Thr Asp Ala	
100 105 110	
aaa act atc caa act aag ctt gag aaa ctt aac gga gtt gaa aaa gtg	384
Lys Thr Ile Gln Thr Lys Leu Glu Lys Leu Asn Gly Val Glu Lys Val	
115 120 125	
act ctt tct gac cat gaa cac aca cca cac tat gta cct atg gac gat	432
Thr Leu Ser Asp His Glu His Thr Pro His Tyr Val Pro Met Asp Asp	
130 135 140	

38 / 63

gaa tta gta tca acc tta cta gct gtc tat gaa aag caa act ggt ctt	480
Glu Leu Val Ser Thr Leu Leu Ala Val Tyr Glu Lys Gln Thr Gly Leu	
145 150 155 160	
aaa gga cat gaa cag gtt att ggt ggt ggg aca ttt ggt cgc tta ctt	528
Lys Gly His Glu Gln Val Ile Gly Gly Gly Thr Phe Gly Arg Leu Leu	
165 170 175	
gaa cgg ggt gtt gca tac ggt gcc atg ttc cca gga gat gaa aac act	576
Glu Arg Gly Val Ala Tyr Gly Ala Met Phe Pro Gly Asp Glu Asn Thr	
180 185 190	
atg cat caa gct aat gag tac atg cct tta gaa aat att ttc cgt tcg	624
Met His Gln Ala Asn Glu Tyr Met Pro Leu Glu Asn Ile Phe Arg Ser	
195 200 205	
gct gct atc tac gca gaa gct atc tat gaa tta atc aaa taaaataatc	673
Ala Ala Ile Tyr Ala Glu Ala Ile Tyr Glu Leu Ile Lys	
210 215 220	
cttaaaactaa atatgtgatc aatgataaag ggtggtgaag acatgaaagt gtctttgcct	733
cttttcataa ggtagattt ggagacttt atg act gac ttg gaa aaa att att	786
Met Thr Asp Leu Glu Lys Ile Ile	
225	
aaa gca ata aaa agt gat tca cag aat caa aat tat aca gaa aat ggt	834
Lys Ala Ile Lys Ser Asp Ser Gln Asn Gln Asn Tyr Thr Glu Asn Gly	
230 235 240 245	
att gat cct ttg ttt gct gct cct aaa aca gct agg atc aat att gtt	882
Ile Asp Pro Leu Phe Ala Ala Pro Lys Thr Ala Arg Ile Asn Ile Val	
250 255 260	
ggc caa gca cct ggt tta aaa act caa gaa gca aga ctc tat tgg aaa	930
Gly Gln Ala Pro Gly Leu Lys Thr Gln Glu Ala Arg Leu Tyr Trp Lys	
265 270 275	
gat aaa tct gga gat cgt cta cgc cag tgg ctt gga gtt gat gaa gag	978
Asp Lys Ser Gly Asp Arg Leu Arg Gln Trp Leu Gly Val Asp Glu Glu	
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Thr Phe Tyr His Ser Gly Lys Phe Ala Val Leu Pro Leu Asp Phe Tyr	
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tac cca ggc aaa gga aaa tca gga gat tta ccc cct aga aaa ggt ttt	1074
Tyr Pro Gly Lys Gly Lys Ser Gly Asp Leu Pro Pro Arg Lys Gly Phe	
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Ala Glu Lys Trp His Pro Leu Ile Leu Lys Glu Met Pro Asn Val Gln	
330 335 340	
ttg acc ttg cta gtt ggt cag tat gct cag aaa tat tat ctt gga agc	1170
Leu Thr Leu Leu Val Gly Gln Tyr Ala Gln Lys Tyr Tyr Leu Gly Ser	
345 350 355	

39 / 63

tcc gca cat aaa aat cta aca gaa aca gtt aaa gct tac aaa gac tat	1218
Ser Ala His Lys Asn Leu Thr Glu Thr Val Lys Ala Tyr Lys Asp Tyr	
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cta ccc gat tat tta ccc ctg gtt cac cca tca ccg cga aat caa att	1266
Leu Pro Asp Tyr Leu Pro Leu Val His Pro Ser Pro Arg Asn Gln Ile	
375 380 385	
tgg cta aag aag aat cca tgg ttt gaa aaa gat cta atc gtt gat tta	1314
Trp Leu Lys Lys Asn Pro Trp Phe Glu Lys Asp Leu Ile Val Asp Leu	
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caa aag ata gta gca gat att tta aaa gat taaggatagg agttgggt atg	1364
Gln Lys Ile Val Ala Asp Ile Leu Lys Asp Met	
410 415	
aga gat aat cat cta cac acg tat ttt tcc tat gat tgt caa acg gca	1412
Arg Asp Asn His Leu His Thr Tyr Phe Ser Tyr Asp Cys Gln Thr Ala	
420 425 430	
ttt gag gac tat att aat ggt ttt aca ggt gaa ttt atc acg aca gaa	1460
Phe Glu Asp Tyr Ile Asn Gly Phe Thr Gly Glu Phe Ile Thr Thr Glu	
435 440 445	
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His Phe Asp Leu Ser Asn Pro Tyr Thr Gly Gln Asp Asp Val Pro Asp	
450 455 460	
tat agt gct tat tgt caa aaa ata gat tat ctt aat cag aaa tat gga	1556
Tyr Ser Ala Tyr Cys Gln Lys Ile Asp Tyr Leu Asn Gln Lys Tyr Gly	
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Asn Arg Phe Lys Lys Gly Ile Glu Ile Gly Tyr Phe Lys Asp Arg Glu	
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Ser Asp Ile Leu Asp Tyr Leu Lys Asn Lys Glu Phe Asp Leu Lys Leu	
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Leu Ser Ile His His Asn Gly Arg Tyr Asp Tyr Leu Gln Glu Glu Ala	
515 520 525	
ctg aaa gta cca aca aag gga gct ttt agc aga tta ctt taatcgtatg	1749
Leu Lys Val Pro Thr Lys Gly Ala Phe Ser Arg Leu Leu	
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caaggtctgc taaaggacta tcaaatgat gaaaatcatt tgatatgagg aaatttttga	2109
taaaaaagct aggcaatatt gcttagcttt tttgtaatgc tattgatagt tttagtgaia	2169

40/63

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tttattggta	acaattcatt	aaaaaaggag	aatgat	atg	aaa aga aaa gac tta	2283
				Met	Lys Arg Lys Asp Leu	
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ttt ggt gat	aaa caa act	caa tac acg	att aga aag	tta agt gtt	gga	2331
Phe Gly Asp	Lys Gln Thr	Gln Tyr Thr	Ile Arg Lys	Leu Ser Val	Gly	
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gta gct tca	gtt aca aca	ggg gta tgt	att ttt ctt	cat agt cca	cag	2379
Val Ala Ser	Val Thr Thr	Gly Val Cys	Ile Phe Leu	His Ser Pro	Gln	
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gta ttt gct	gaa gaa gta	agt gtt tct	cct gca act	aca gcg att	gca	2427
Val Phe Ala	Glu Glu Val	Ser Val Ser	Pro Ala Thr	Thr Ala Ile	Ala	
	580		585		590	
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Glu Ser Asn	Ile Asn Gln	Val Asp Asn	Gln Gln Ser	Thr Asn Leu	Lys	
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gat gac ata	aac tca aac	tct gag acg	gtt gtg aca	ccc tca gat	atg	2523
Asp Asp Ile	Asn Ser Asn	Ser Glu Thr	Val Val Thr	Pro Ser Asp	Met	
	615		620		625	
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Pro Asp Thr	Lys Gln Leu	Val Ser Asp	Glu Thr Asp	Thr Gln Lys	Gly	
	630		635		640	
gtg aca gag	ccg gat aag	gcg aca agc	ctg ctt gaa	gaa aat aaa	ggc	2619
Val Thr Glu	Pro Asp Lys	Ala Thr Ser	Leu Leu Glu	Glu Asn Lys	Gly	
	645		650		655	
cct gtt tca	gat aaa aat	acc tta gat	tta aaa gta	gca cca tct	aca	2667
Pro Val Ser	Asp Lys Asn	Thr Leu Asp	Leu Lys Val	Ala Pro Ser	Thr	
	660		665		670	
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Leu Gln Asn	Thr Pro Asp	Lys Thr Ser	Gln Ala Ile	Gly Ala Pro	Ser	
	680		685		690	
cct acc ttg	aaa gta gct	aat caa gct	cca cgg att	gaa aat ggc	tac	2763
Pro Thr Leu	Lys Val Ala	Asn Gln Ala	Pro Arg Ile	Glu Asn Gly	Tyr	
	695		700		705	
ttt agg cta	cat ctt aaa	gaa ttg cct	caa ggt cat	cct gta gaa	agc	2811
Phe Arg Leu	His Leu Lys	Glu Leu Pro	Gln Gly His	Pro Val Glu	Ser	
	710		715		720	
act gga ctt	tgg ata tgg	gga gat gtt	gat caa ccg	tct agt aat	tgg	2859
Thr Gly Leu	Trp Ile Trp	Gly Asp Val	Asp Gln Pro	Ser Ser Asn	Trp	
	725		730		735	
cca aat ggt	gct atc cct	atg act gat	gct aag aaa	gat gat tac	ggc	2907
Pro Asn Gly	Ala Ile Pro	Met Thr Asp	Ala Lys Lys	Asp Asp Tyr	Gly	
	740		745		750	
					755	

41 / 63

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Tyr Tyr Val Asp Phe Lys Leu Ser Glu Lys Gln Arg Lys Gln Ile Ser	
760 765 770	
ttt tta att aat aac aaa gca ggg aca aat tta agc ggc gat cat cat	3003
Phe Leu Ile Asn Asn Lys Ala Gly Thr Asn Leu Ser Gly Asp His His	
775 780 785	
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Ile Pro Leu Leu Arg Pro Glu Met Asn Gln Val Trp Ile Asp Glu Lys	
790 795 800	
tac ggt ata cat act tat caa ccc ctc aaa gaa ggg tat gtc cgt att	3099
Tyr Gly Ile His Thr Tyr Gln Pro Leu Lys Glu Gly Tyr Val Arg Ile	
805 810 815	
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Asn Tyr Leu Ser Ser Ser Ser Asn Tyr Asp His Leu Ser Ala Trp Leu	
820 825 830 835	
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Phe Lys Asp Val Ala Thr Xaa Ser Thr Thr Trp Pro Asp Gly Ser Asn	
840 845 850	
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Phe Val Asn Gln Gly Leu Tyr Gly Arg Tyr Ile Asp Val Ser Leu Lys	
855 860 865	
act aac gcc aaa gag att ggt ttt cta atc tta gat gaa agt aag aca	3291
Thr Asn Ala Lys Glu Ile Gly Phe Leu Ile Leu Asp Glu Ser Lys Thr	
870 875 880	
gga gat gca gtg aaa gtt caa ccc aac gac tat gtt ttt aga gat tta	3339
Gly Asp Ala Val Lys Val Gln Pro Asn Asp Tyr Val Phe Arg Asp Leu	
885 890 895	
gct aac cat aac caa att ttt gta aaa gat aag gat cca aag gtt tat	3387
Ala Asn His Asn Gln Ile Phe Val Lys Asp Lys Asp Pro Lys Val Tyr	
900 905 910 915	
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Asn Asn Pro Tyr Tyr Ile Asp Gln Val Gln Leu Lys Asp Ala Gln Gln	
920 925 930	
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Ile Asp Leu Thr Ser Ile Gln Ala Ser Phe Thr Thr Leu Asp Gly Val	
935 940 945	
gat aaa act gaa att tta aaa gaa ttg aaa gtg act gat aaa aat caa	3531
Asp Lys Thr Glu Ile Leu Lys Glu Leu Lys Val Thr Asp Lys Asn Gln	
950 955 960	
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Asn Ala Ile Gln Ile Ser Asp Ile Thr Leu Asp Thr Ser Lys Ser Leu	
965 970 975	

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Leu Ile Ile Lys Gly Asp Phe Asn Pro Lys Gln Gly His Phe Asn Ile	
980 985 990 995	
tct tat aat ggt aac aat gtc atg aca agg caa tct tgg gaa ttt aaa	3675
Ser Tyr Asn Gly Asn Asn Val Met Thr Arg Gln Ser Trp Glu Phe Lys	
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gac caa ctt tat gct tat agt gga aat tta ggt gca gtt ctc aat caa	3723
Asp Gln Leu Tyr Ala Tyr Ser Gly Asn Leu Gly Ala Val Leu Asn Gln	
1015 1020 1025	
gat ggt tca aaa gtt gaa gcc agc ctc tgg tca ccg agt gct gat agt	3771
Asp Gly Ser Lys Val Glu Ala Ser Leu Trp Ser Pro Ser Ala Asp Ser	
1030 1035 1040	
gtc act atg att att tat gac aaa gat aac caa aac agg gtt gta gcg	3819
Val Thr Met Ile Ile Tyr Asp Lys Asp Asn Gln Asn Arg Val Val Ala	
1045 1050 1055	
act acc ccc ctt gtg aaa aat aat aaa ggt gtt tgg cag acg ata ctt	3867
Thr Thr Pro Leu Val Lys Asn Asn Lys Gly Val Trp Gln Thr Ile Leu	
1060 1065 1070 1075	
gat act aaa tta ggt att aaa aac tat act ggt tac tat tat ctt tac	3915
Asp Thr Lys Leu Gly Ile Lys Asn Tyr Thr Gly Tyr Tyr Tyr Leu Tyr	
1080 1085 1090	
gaa ata aaa aga ggt aag gat aag gtt aag att tta gat cct tat gca	3963
Glu Ile Lys Arg Gly Lys Asp Lys Val Lys Ile Leu Asp Pro Tyr Ala	
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aag tca tta gca gag tgg gat agt aat act gtt aat gat gat att aaa	4011
Lys Ser Leu Ala Glu Trp Asp Ser Asn Thr Val Asn Asp Asp Ile Lys	
1110 1115 1120	
acg gct aaa gca gct ttt gta aat cca agt caa ctt gga cct caa aat	4059
Thr Ala Lys Ala Ala Phe Val Asn Pro Ser Gln Leu Gly Pro Gln Asn	
1125 1130 1135	
tta agt ttt gct aaa att gct aat ttt aaa gga aga caa gat gct gtt	4107
Leu Ser Phe Ala Lys Ile Ala Asn Phe Lys Gly Arg Gln Asp Ala Val	
1140 1145 1150 1155	
ata tac gaa gca cat gta aga gac ttc act tct gat cga tct ttg gat	4155
Ile Tyr Glu Ala His Val Arg Asp Phe Thr Ser Asp Arg Ser Leu Asp	
1160 1165 1170	
gga aaa tta aaa aat caa ttt ggt acc ttt gca gcc ttt tca gag aaa	4203
Gly Lys Leu Lys Asn Gln Phe Gly Thr Phe Ala Ala Phe Ser Glu Lys	
1175 1180 1185	
cta gat tat tta cag aaa tta gga gtt aca cac att cag ctt tta ccg	4251
Leu Asp Tyr Leu Gln Lys Leu Gly Val Thr His Ile Gln Leu Leu Pro	
1190 1195 1200	

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Val Leu Ser Tyr Phe Tyr Val Asn Glu Met Asp Lys Ser Arg Ser Thr	
1205 1210 1215	
gct tac act tcc tca gac aat aat tac aat tgg ggc tat gac cca cag	4347
Ala Tyr Thr Ser Ser Asp Asn Asn Tyr Asn Trp Gly Tyr Asp Pro Gln	
1220 1225 1230 1235	
agc tat ttt gct ctt tct ggg atg tat tca gag aaa cca aaa gat cca	4395
Ser Tyr Phe Ala Leu Ser Gly Met Tyr Ser Glu Lys Pro Lys Asp Pro	
1240 1245 1250	
tca gca cgt atc gcc gaa tta aaa caa tta ata cat gat att cat aaa	4443
Ser Ala Arg Ile Ala Glu Leu Lys Gln Leu Ile His Asp Ile His Lys	
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cgt ggc atg ggg gtt ata ctt gat gtc gtc tat aat cac act gca aaa	4491
Arg Gly Met Gly Val Ile Leu Asp Val Val Tyr Asn His Thr Ala Lys	
1270 1275 1280	
act tat ctc ttt gag gat ata gaa cct aat tat tat cac ttt atg aat	4539
Thr Tyr Leu Phe Glu Asp Ile Glu Pro Asn Tyr Tyr His Phe Met Asn	
1285 1290 1295	
gaa gat ggt tca cca aga gaa agt ttt gga ggg gga cgt tta gga acc	4587
Glu Asp Gly Ser Pro Arg Glu Ser Phe Gly Gly Gly Arg Leu Gly Thr	
1300 1305 1310 1315	
act cat gca atg agt cgt cgt gtt ttg gtt gat tcc att aaa tat ctt	4635
Thr His Ala Met Ser Arg Arg Val Leu Val Asp Ser Ile Lys Tyr Leu	
1320 1325 1330	
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Thr Ser Glu Phe Lys Val Asp Gly Phe Arg Phe Asp Met Met Gly Asp	
1335 1340 1345	
cat gat gcg gct gcg att gaa tta gct tat aaa gaa gct aaa gct att	4731
His Asp Ala Ala Ala Ile Glu Leu Ala Tyr Lys Glu Ala Lys Ala Ile	
1350 1355 1360	
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Asn Pro Asn Met Ile Met Ile Gly Glu Gly Trp Arg Thr Phe Gln Gly	
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Asp Gln Gly Gln Pro Val Lys Pro Ala Asp Gln Asp Trp Met Lys Ser	
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Ser Gly Phe Pro Asn Glu Gly Thr Pro Ala Phe Ile Thr Gly Gly Pro	
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44 / 63

caa tct tta caa ggt att ttt aaa aat atc aaa gca caa cct ggg aat 4971
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ttt gaa gca gat tcg cca gga gat gtg gtg cag tat att gct gca cat 5019
 Phe Glu Ala Asp Ser Pro Gly Asp Val Val Gln Tyr Ile Ala Ala His
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 35 40 45
 Pro Ala Arg Ala Phe Leu Asp Val Thr Ala Asn Ile Ile His Glu Asp
 50 55 60
 Phe Ser Gly Glu Lys Leu Gly Val Ala Tyr Glu Asp Asp Cys Met Gly
 65 70 75 80
 Pro Leu Ser Met Asn Ala Gly Val Phe Gln Phe Asp Glu Thr Asn Asp
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 Asp Asn Thr Ile Ala Leu Asn Phe Arg Tyr Pro Gln Gly Thr Asp Ala
 100 105 110
 Lys Thr Ile Gln Thr Lys Leu Glu Lys Leu Asn Gly Val Glu Lys Val
 115 120 125
 Thr Leu Ser Asp His Glu His Thr Pro His Tyr Val Pro Met Asp Asp
 130 135 140
 Glu Leu Val Ser Thr Leu Leu Ala Val Tyr Glu Lys Gln Thr Gly Leu
 145 150 155 160
 Lys Gly His Glu Gln Val Ile Gly Gly Gly Thr Phe Gly Arg Leu Leu
 165 170 175
 Glu Arg Gly Val Ala Tyr Gly Ala Met Phe Pro Gly Asp Glu Asn Thr
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 Met His Gln Ala Asn Glu Tyr Met Pro Leu Glu Asn Ile Phe Arg Ser
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<400> 24

45/63

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Lys Thr Ala Arg Ile Asn Ile Val Gly Gln Ala Pro Gly Leu Lys Thr
 35          40          45
Gln Glu Ala Arg Leu Tyr Trp Lys Asp Lys Ser Gly Asp Arg Leu Arg
 50          55          60
Gln Trp Leu Gly Val Asp Glu Glu Thr Phe Tyr His Ser Gly Lys Phe
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Ala Val Leu Pro Leu Asp Phe Tyr Tyr Pro Gly Lys Gly Lys Ser Gly
 85          90          95
Asp Leu Pro Pro Arg Lys Gly Phe Ala Glu Lys Trp His Pro Leu Ile
 100         105         110
Leu Lys Glu Met Pro Asn Val Gln Leu Thr Leu Leu Val Gly Gln Tyr
 115         120         125
Ala Gln Lys Tyr Tyr Leu Gly Ser Ser Ala His Lys Asn Leu Thr Glu
 130         135         140
Thr Val Lys Ala Tyr Lys Asp Tyr Leu Pro Asp Tyr Leu Pro Leu Val
 145         150         155         160
His Pro Ser Pro Arg Asn Gln Ile Trp Leu Lys Lys Asn Pro Trp Phe
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Lys Asp

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<213> streptococcus

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Glu His Phe Asp Leu Ser Asn Pro Tyr Thr Gly Gln Asp Asp Val Pro
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Asp Tyr Ser Ala Tyr Cys Gln Lys Ile Asp Tyr Leu Asn Gln Lys Tyr
 50          55          60
Gly Asn Arg Phe Lys Lys Gly Ile Glu Ile Gly Tyr Phe Lys Asp Arg
 65          70          75          80
Glu Ser Asp Ile Leu Asp Tyr Leu Lys Asn Lys Glu Phe Asp Leu Lys
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46/63

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Ala	Thr	Thr	Ala	Ile	Ala	Glu	Ser	Asn	Ile	Asn	Gln	Val	Asp	Asn	Gln
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Gln	Ser	Thr	Asn	Leu	Lys	Asp	Asp	Ile	Asn	Ser	Asn	Ser	Glu	Thr	Val
65				70					75					80	
Val	Thr	Pro	Ser	Asp	Met	Pro	Asp	Thr	Lys	Gln	Leu	Val	Ser	Asp	Glu
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Thr	Asp	Thr	Gln	Lys	Gly	Val	Thr	Glu	Pro	Asp	Lys	Ala	Thr	Ser	Leu
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Leu	Glu	Glu	Asn	Lys	Gly	Pro	Val	Ser	Asp	Lys	Asn	Thr	Leu	Asp	Leu
		115				120						125			
Lys	Val	Ala	Pro	Ser	Thr	Leu	Gln	Asn	Thr	Pro	Asp	Lys	Thr	Ser	Gln
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Ala	Ile	Gly	Ala	Pro	Ser	Pro	Thr	Leu	Lys	Val	Ala	Asn	Gln	Ala	Pro
145				150					155						160
Arg	Ile	Glu	Asn	Gly	Tyr	Phe	Arg	Leu	His	Leu	Lys	Glu	Leu	Pro	Gln
			165					170						175	
Gly	His	Pro	Val	Glu	Ser	Thr	Gly	Leu	Trp	Ile	Trp	Gly	Asp	Val	Asp
		180						185					190		
Gln	Pro	Ser	Ser	Asn	Trp	Pro	Asn	Gly	Ala	Ile	Pro	Met	Thr	Asp	Ala
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Lys	Lys	Asp	Asp	Tyr	Gly	Tyr	Tyr	Val	Asp	Phe	Lys	Leu	Ser	Glu	Lys
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Gln	Arg	Lys	Gln	Ile	Ser	Phe	Leu	Ile	Asn	Asn	Lys	Ala	Gly	Thr	Asn
225				230					235						240
Leu	Ser	Gly	Asp	His	His	Ile	Pro	Leu	Leu	Arg	Pro	Glu	Met	Asn	Gln
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Val	Trp	Ile	Asp	Glu	Lys	Tyr	Gly	Ile	His	Thr	Tyr	Gln	Pro	Leu	Lys
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Glu	Gly	Tyr	Val	Arg	Ile	Asn	Tyr	Leu	Ser	Ser	Ser	Ser	Asn	Tyr	Asp
	275						280					285			
His	Leu	Ser	Ala	Trp	Leu	Phe	Lys	Asp	Val	Ala	Thr	Xaa	Ser	Thr	Thr
	290					295					300				
Trp	Pro	Asp	Gly	Ser	Asn	Phe	Val	Asn	Gln	Gly	Leu	Tyr	Gly	Arg	Tyr
305				310					315						320
Ile	Asp	Val	Ser	Leu	Lys	Thr	Asn	Ala	Lys	Glu	Ile	Gly	Phe	Leu	Ile
			325					330						335	
Leu	Asp	Glu	Ser	Lys	Thr	Gly	Asp	Ala	Val	Lys	Val	Gln	Pro	Asn	Asp
		340						345					350		
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47 / 63

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Ala	Ala	Phe	Ser	Glu	Lys	Leu	Asp	Tyr	Leu	Gln	Lys	Leu	Gly	Val	Thr
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His	Ile	Gln	Leu	Leu	Pro	Val	Leu	Ser	Tyr	Phe	Tyr	Val	Asn	Glu	Met
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48/63

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50 / 63

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<213> streptococcus

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Gly Val Glu Arg Thr Phe Pro Ile His Thr Pro Arg Val Asp Lys Ile
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20           25           30
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35           40           45
Ile Asp Asn Asp Thr Leu Phe Phe Leu His Glu Phe Thr Lys Asn Lys

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51/63

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	85	90
Thr Phe Ala Ser Tyr Leu Ile Ser Ile Ser Gln Val Leu Asp His Glu		95
	100	105
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	115	120
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52/63

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<210> 33
<211> 649
<212> PRT
<213> Streptococcus
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Lys	Ser	Gly	Asn 20	Thr	Leu	Ile	Asp	Gln 25	Leu	Val	Ala	Asp	Gly 30	Leu	Leu
His	Ala	Asp 35	Asn	His	Tyr	His	Phe 40	Phe	Asn	Gly	Lys	Ser	Leu 45	Ala	Thr
Phe	Asn 50	Thr	Asn	Gln	Leu	Ile 55	Arg	Glu	Val	Val	Tyr 60	Val	Glu	Ile	Ser
Leu 65	Asp	Thr	Met	Ser	Ser 70	Gly	Glu	His	Asp	Leu 75	Val	Lys	Val	Asn 80	Ile
Ile	Arg	Pro	Thr 85	Thr	Glu	His	Thr	Ile	Pro 90	Thr	Met	Met	Thr 95	Ala	Ser
Pro	Tyr	His	Gln 100	Gly	Ile	Asn	Asp	Pro 105	Ala	Ala	Asp	Gln	Lys 110	Thr	Tyr
Gln	Met	Glu	Gly 115	Ala	Leu	Ala	Val	Lys 120	Gln	Pro	Lys	His 125	Ile	Gln	Val
Asp	Thr 130	Lys	Pro	Phe	Lys	Glu	Glu	Val 135	Lys	His	Pro 140	Ser	Lys	Leu	Pro
Ile 145	Ser	Pro	Ala	Thr	Glu	Ser	Phe	Thr	His	Ile	Asp	Ser	Tyr	Ser	Leu
Asn	Asp	Tyr	Phe 165	Leu	Ser	Arg	Gly	Phe	Ala 170	Asn	Ile	Tyr	Val	Ser 175	Gly
Val	Gly	Thr	Ala 180	Gly	Ser	Thr	Gly	Phe 185	Met	Thr	Ser	Gly	Asp 190	Tyr	Gln
Gln	Ile	Gln	Ser 195	Phe	Lys	Ala	Val	Ile 200	Asp	Trp	Leu	Asn	Gly 205	Lys	Val
Thr	Ala 210	Phe	Thr	Ser	His	Lys	Arg	Asp 215	Lys	Gln	Val	Lys	Ala 220	Asp	Trp
Ser 225	Asn	Gly	Leu	Val	Ala	Thr	Thr	Gly	Lys	Ser	Tyr	Leu	Gly 235	Thr	Met
Ser	Thr	Gly	Leu	Ala	Thr	Thr	Gly	Val	Glu	Gly	Leu	Lys	Val 245	Ile	Ile
Ala	Glu	Ala	Ala 260	Ile	Ser	Thr	Trp	Tyr	Asp	Tyr	Tyr	Arg	Glu 270	Asn	Gly
Leu	Val	Cys	Ser 275	Pro	Gly	Gly	Tyr	Pro 280	Gly	Glu	Asp	Leu	Asp 285	Val	Leu
Thr	Glu 290	Leu	Thr	Tyr	Ser	Arg	Asn	Leu	Leu	Ala	Gly	Asp	Tyr 300	Ile	Lys
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55/63

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305          310          315          320
Asp Arg Gln Ser Gly Asp Tyr Asn Gln Tyr Trp His Asp Arg Asn Tyr
          325          330          335
Leu Thr His Val Asn Asn Val Lys Ser Arg Val Val Tyr Thr His Gly
          340          345          350
Leu Gln Asp Trp Asn Val Lys Pro Arg His Val Tyr Lys Val Phe Asn
          355          360          365
Ala Leu Pro Gln Thr Ile Lys Lys His Leu Phe Leu His Gln Gly Gln
          370          375          380
His Val Tyr Met His Asn Trp Gln Ser Ile Asp Phe Arg Glu Ser Met
385          390          395          400
Asn Ala Leu Leu Ser Gln Glu Leu Leu Gly Ile Asp Asn His Phe Gln
          405          410          415
Leu Glu Glu Val Ile Trp Gln Asp Asn Thr Thr Glu Gln Thr Trp Gln
          420          425          430
Val Leu Asp Ala Phe Gly Gly Asn His Gln Glu Gln Ile Gly Leu Gly
          435          440          445
Asp Ser Lys Lys Leu Ile Asp Asn His Tyr Asp Lys Glu Ala Phe Asp
          450          455          460
Thr Tyr Cys Lys Asp Phe Asn Val Phe Lys Asn Asp Leu Phe Lys Gly
465          470          475          480
Asn Asn Lys Thr Asn Gln Ile Thr Ile Asn Leu Pro Leu Lys Lys Asn
          485          490          495
Tyr Leu Leu Asn Gly Gln Cys Lys Leu His Leu Arg Val Lys Thr Ser
          500          505          510
Asp Lys Lys Ala Ile Leu Ser Ala Gln Ile Leu Asp Tyr Gly Pro Lys
          515          520          525
Lys Arg Phe Lys Asp Thr Pro Thr Ile Lys Phe Leu Asn Ser Leu Asp
          530          535          540
Asn Gly Lys Asn Phe Ala Arg Glu Ala Leu Arg Glu Leu Pro Phe Thr
545          550          555          560
Lys Asp His Tyr Arg Val Ile Ser Lys Gly Val Leu Asn Leu Gln Asn
          565          570          575
Arg Thr Asp Leu Leu Thr Ile Glu Ala Ile Glu Pro Glu Gln Trp Phe
          580          585          590
Asp Ile Glu Phe Ser Leu Gln Pro Ser Ile Tyr Gln Leu Ser Lys Gly
          595          600          605
Asp Asn Leu Arg Ile Ile Leu Tyr Thr Thr Asp Phe Glu His Thr Ile
          610          615          620
Arg Asp Asn Ala Ser Tyr Ser Ile Thr Val Asp Leu Ser Gln Ser Tyr
625          630          635          640
Leu Thr Ile Pro Thr Asn Gln Gly Asn
          645

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<210> 34
<211> 119
<212> PRT
<213> Streptococcus

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<400> 34
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Tyr Gln Ile Asn Leu Leu Gln Glu Ser Asn Phe Gly Ala Val Phe Asp
          20          25          30
His Asp Asn Lys Asn Ile Pro Gln Val Val Ala Thr Ile Val Asp Asp
          35          40          45

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56 / 63

Leu Gln Gly Ser Gly Ser Ser Asn His Phe Trp Tyr Phe Gly Asn Thr
 50 55 60
 Thr Asp Thr Ser Ile Leu Met Ile Ala His Leu Asn Arg Lys Phe Tyr
 65 70 75 80
 Ile Gln Val Asn Leu Lys Asp Phe Asp Phe Ala Leu Asn Leu Ile Ala
 85 90 95
 Ile Asn Asn Trp Lys Ser Leu Leu Gln Thr Gln Leu Glu Ala Leu Asn
 100 105 110
 Asp Thr Leu Ala Ile Phe Gln
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<210> 35
 <211> 326
 <212> PRT
 <213> Streptococcus

<400> 35
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 Glu Thr Asn Gln Leu Ile Gln Glu Arg Ile Gln Val Arg Asn Lys Asp
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 Ile Glu Ala Ala Leu Ser Gln Leu Thr Ala Ala Gly Gly Lys Gln Leu
 35 40 45
 Arg Pro Ala Phe Phe Tyr Leu Phe Ser Gln Leu Gly Asn Lys Glu Asn
 50 55 60
 Gln Asp Thr Gln Gln Leu Lys Lys Ile Ala Ala Ser Leu Glu Ile Leu
 65 70 75 80
 His Val Ala Thr Leu Ile His Asp Asp Val Ile Asp Asp Ser Pro Leu
 85 90 95
 Arg Arg Gly Asn Met Thr Ile Gln Ser Lys Phe Gly Lys Asp Ile Ala
 100 105 110
 Val Tyr Thr Gly Asp Leu Leu Phe Thr Val Phe Phe Asp Leu Ile Leu
 115 120 125
 Glu Ser Met Thr Asp Thr Pro Phe Met Arg Ile Asn Ala Lys Ser Met
 130 135 140
 Arg Lys Ile Leu Met Gly Glu Leu Asp Gln Met His Leu Arg Tyr Asn
 145 150 155 160
 Gln Gln Gln Gly Ile His His Tyr Leu Arg Ala Ile Ser Gly Lys Thr
 165 170 175
 Ala Glu Leu Phe Lys Leu Ala Ser Lys Glu Gly Ala Tyr Phe Gly Gly
 180 185 190
 Ala Glu Lys Glu Val Val Arg Leu Ala Gly His Ile Gly Phe Asn Ile
 195 200 205
 Gly Met Thr Phe Gln Ile Leu Asp Asp Ile Leu Asp Tyr Thr Ala Asp
 210 215 220
 Lys Lys Thr Phe Asn Lys Pro Val Leu Glu Asp Leu Thr Gln Gly Val
 225 230 235 240
 Tyr Ser Leu Pro Leu Leu Leu Ala Ile Glu Glu Asn Pro Asp Ile Phe
 245 250 255
 Lys Pro Ile Leu Asp Lys Lys Thr Asp Met Ala Thr Glu Asp Met Glu
 260 265 270
 Lys Ile Ala Tyr Leu Val Val Ser His Arg Gly Val Asp Lys Ala Arg
 275 280 285
 His Leu Ala Arg Lys Phe Thr Glu Lys Ala Ile Ser Asp Ile Asn Lys
 290 295 300
 Leu Pro Gln Asn Ser Ala Lys Lys Gln Leu Leu Gln Leu Thr Asn Tyr


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<210> 36
<211> 247
<212> PRT
<213> Streptococcus
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Tyr	Lys	Pro	Gln 20	Glu	Lys	Trp	Val	Leu 25	His	His	Leu	Asp 30	Leu	Asp	Ile				
Lys	Glu	Gly 35	Glu	Lys	Ile	Ala	Ile 40	Leu	Gly	Arg	Ser	Gly 45	Ser	Gly	Lys				
Ser	Thr 50	Leu	Ala	Ser	Leu	Leu 55	Arg	Gly	Asp	Leu	Lys 60	Ala	Ser	Gln	Gly				
Lys 65	Ile	Thr	Leu	Gly 70	Gly	Ala	Asp	Val	Ser	Ile 75	Val	Gly	Asp	Cys 80	Ile				
Ser	Asn	Tyr	Ile 85	Gly	Val	Ile	Gln	Gln 90	Ala	Pro	Tyr	Leu	Phe 95	Asn	Thr				
Thr	Leu	Leu	Asn 100	Asn	Ile	Arg	Ile	Gly 105	Asn	Gln	Asp	Ala 110	Ser	Glu	Glu				
Asp	Val	Trp 115	Lys	Val	Leu	Glu	Arg 120	Val	Gly	Leu	Lys 125	Glu	Met	Val	Thr				
Asp 130	Leu	Ser	Asp	Gly 135	Leu	Tyr	Thr 140	Met	Val	Asp	Glu 145	Ala	Gly	Leu	Arg				
Phe 145	Ser	Gly	Gly 150	Glu	Arg	His	Arg 155	Ile	Ala	Leu	Ala 160	Arg	Ile	Leu	Leu				
Lys	Asp	Val	Pro 165	Ile	Val	Ile	Leu 170	Asp	Glu	Pro	Thr 175	Val	Gly	Leu	Asp				
Pro	Ile	Thr 180	Glu	Gln	Ala	Leu	Leu 185	Arg	Val	Phe	Met 190	Lys	Glu	Leu	Glu				
Gly	Lys 195	Thr	Leu	Val	Trp	Ile 200	Thr	His	His	Leu	Lys 205	Gly	Ile	Glu	His				
Ala	Asp 210	Arg	Ile	Leu	Phe	Ile 215	Glu	Asn	Gly	Gln	Leu 220	Glu	Leu	Glu	Gly				
Ser 225	Pro	Gln	Glu	Leu 230	Ser	Gln	Ser	Ser	Gln	Arg 235	Tyr	Arg	Gln	Leu	Lys 240				
Ala	Ala	Asp	Asp 245	Gly	Asp	Leu													

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<210> 37
<211> 3480
<212> DNA
<213> Streptococcus
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<400> 37						
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<210> 38

<211> 306

<212> PRT

<213> Streptococcus

59 / 63

<400> 38

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Leu Ala Asp Thr Tyr Val Arg Pro Ile Asp Asn Gly Arg Ile Thr Thr
          35          40          45
Gly Phe Asn Gly Tyr Pro Gly His Cys Gly Val Asp Tyr Ala Val Pro
          50          55          60
Thr Gly Thr Ile Ile Arg Ala Val Ala Asp Gly Thr Val Lys Phe Ala
65          70          75          80
Gly Ala Gly Ala Asn Phe Ser Trp Met Thr Asp Leu Ala Gly Asn Cys
          85          90          95
Val Met Ile Gln His Ala Asp Gly Met His Ser Gly Tyr Ala His Met
          100          105          110
Ser Arg Val Val Ala Arg Thr Gly Glu Lys Val Lys Gln Gly Asp Ile
          115          120          125
Ile Gly Tyr Val Gly Ala Thr Gly Met Ala Thr Gly Pro His Leu His
          130          135          140
Phe Glu Phe Leu Pro Ala Asn Pro Asn Phe Gln Asn Gly Phe His Gly
145          150          155          160
Arg Ile Asn Pro Thr Ser Leu Ile Ala Asn Val Ala Thr Phe Ser Gly
          165          170          175
Lys Thr Gln Ala Ser Ala Pro Ser Ile Lys Pro Leu Gln Ser Ala Pro
          180          185          190
Val Gln Asn Gln Ser Ser Lys Leu Lys Val Tyr Arg Val Asp Glu Leu
          195          200          205
Gln Lys Val Asn Gly Val Trp Leu Val Lys Asn Asn Thr Leu Thr Pro
          210          215          220
Thr Gly Phe Asp Trp Asn Asp Asn Gly Ile Pro Ala Ser Glu Ile Asp
225          230          235          240
Glu Val Asp Ala Asn Gly Asn Leu Thr Ala Asp Gln Val Leu Gln Lys
          245          250          255
Gly Gly Tyr Phe Ile Phe Asn Pro Lys Thr Leu Lys Thr Val Glu Lys
          260          265          270
Pro Ile Gln Gly Thr Ala Gly Leu Thr Trp Ala Lys Thr Arg Phe Ala
          275          280          285
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290          295          300
Tyr Lys
305

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<210> 39

<211> 434

<212> PRT

<213> Streptococcus

<400> 39

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Met Lys Met Asn Lys Lys Val Leu Leu Thr Ser Thr Met Ala Ala Ser
 1          5          10          15
Leu Leu Ser Val Ala Ser Val Gln Ala Gln Glu Thr Asp Thr Thr Trp
          20          25          30
Thr Ala Arg Thr Val Ser Glu Val Lys Ala Asp Leu Val Lys Gln Asp
          35          40          45
Asn Lys Ser Ser Tyr Thr Val Lys Tyr Gly Asp Thr Leu Ser Val Ile

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60 / 63

50	55	60
Ser Glu Ala Met Ser Ile Asp Met Asn Val Leu Ala Lys Ile Asn Asn		
65	70	75
Ile Ala Asp Ile Asn Leu Ile Tyr Pro Glu Thr Thr Leu Thr Val Thr		80
	85	90
Tyr Asp Gln Lys Ser His Thr Ala Thr Ser Met Lys Ile Glu Thr Pro		95
	100	105
Ala Thr Asn Ala Ala Gly Gln Thr Thr Ala Thr Val Asp Leu Lys Thr		110
	115	120
Asn Gln Val Ser Val Ala Asp Gln Lys Val Ser Leu Asn Thr Ile Ser		125
	130	135
Glu Gly Met Thr Pro Glu Ala Ala Thr Thr Ile Val Ser Pro Met Lys		140
145	150	155
Thr Tyr Ser Ser Ala Pro Ala Leu Lys Ser Lys Glu Val Leu Ala Gln		160
	165	170
Glu Gln Ala Val Ser Gln Ala Ala Ala Asn Glu Gln Val Ser Thr Ala		175
	180	185
Pro Val Lys Ser Ile Thr Ser Glu Val Pro Ala Ala Lys Glu Glu Val		190
	195	200
Lys Pro Thr Gln Thr Ser Val Ser Gln Ser Thr Thr Val Ser Pro Ala		205
	210	215
Ser Val Ala Ala Glu Thr Pro Ala Pro Val Ala Lys Val Ala Pro Val		220
225	230	235
Arg Thr Val Ala Ala Pro Arg Val Ala Ser Val Lys Val Val Thr Pro		240
	245	250
Lys Val Glu Thr Gly Ala Ser Pro Glu His Val Ser Ala Pro Ala Val		255
	260	265
Pro Val Thr Thr Thr Ser Thr Ala Thr Asp Ser Lys Leu Gln Ala Thr		270
	275	280
Glu Val Lys Ser Val Pro Val Ala Gln Lys Ala Pro Thr Ala Thr Pro		285
	290	295
Val Ala Gln Pro Ala Ser Thr Thr Asn Ala Val Ala Ala His Pro Glu		300
305	310	315
Asn Ala Gly Leu Gln Pro His Val Ala Ala Tyr Lys Glu Lys Val Ala		320
	325	330
Ser Thr Tyr Gly Val Asn Glu Phe Ser Thr Tyr Arg Ala Gly Asp Pro		335
	340	345
Gly Asp His Gly Lys Gly Leu Ala Val Asp Phe Ile Val Gly Lys Asn		350
	355	360
Gln Ala Leu Gly Asn Glu Val Ala Gln Tyr Ser Thr Gln Asn Met Ala		365
	370	375
Ala Asn Asn Ile Ser Tyr Val Ile Trp Gln Gln Lys Phe Tyr Ser Asn		380
385	390	395
Thr Asn Ser Ile Tyr Gly Pro Ala Asn Thr Trp Asn Ala Met Pro Asp		400
	405	410
Arg Gly Gly Val Thr Ala Asn His Tyr Asp His Val His Val Ser Phe		415
	420	425
Asn Lys		430

<210> 40

<211> 232

<212> PRT

<213> Streptococcus

<400> 40

61 / 63

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Met Pro His Leu Ser Lys Glu Ala Phe Lys Lys Gln Ile Lys Asn Gly
 1          5          10          15
Ile Ile Val Ser Cys Gln Ala Leu Pro Gly Glu Pro Leu Tyr Thr Glu
          20          25          30
Ser Gly Gly Val Met Pro Leu Leu Ala Leu Ala Ala Gln Glu Ala Gly
          35          40          45
Ala Val Gly Ile Arg Ala Asn Ser Val Arg Asp Ile Lys Glu Ile Gln
          50          55          60
Glu Val Thr Asn Leu Pro Ile Ile Gly Ile Ile Lys Arg Glu Tyr Pro
65          70          75          80
Pro Gln Glu Pro Phe Ile Thr Ala Thr Met Thr Glu Val Asp Gln Leu
          85          90          95
Ala Ser Leu Asp Ile Ala Val Ile Ala Leu Asp Cys Thr Leu Arg Glu
          100          105          110
Arg His Asp Gly Leu Ser Val Ala Glu Phe Ile Gln Lys Ile Lys Gly
          115          120          125
Lys Tyr Pro Glu Gln Leu Leu Met Ala Asp Ile Ser Thr Phe Glu Glu
          130          135          140
Gly Lys Asn Ala Phe Glu Ala Gly Val Asp Phe Val Gly Thr Thr Leu
145          150          155          160
Ser Gly Tyr Thr Asp Tyr Xaa Arg Gln Glu Glu Gly Pro Asp Ile Glu
          165          170          175
Leu Leu Asn Lys Leu Cys Gln Ala Gly Ile Asp Val Ile Ala Glu Gly
          180          185          190
Lys Ile His Thr Pro Lys Gln Ala Asn Glu Ile Asn His Ile Gly Val
          195          200          205
Ala Gly Ile Val Val Gly Gly Ala Ile Thr Arg Pro Lys Glu Ile Ala
          210          215          220
Glu Arg Phe Ile Ser Gly Leu Ser
225          230

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<210> 41
<211> 39
<212> PRT
<213> Streptococcus

```

```

<400> 41
Met Ser Ile Lys Lys Ser Val Ile Gly Phe Cys Leu Gly Ala Ala Ala
 1          5          10          15
Leu Ser Met Phe Ala Cys Val Asp Ser Ser Gln Ser Val Met Ala Ala
          20          25          30
Glu Lys Asp Lys Val Glu Ile
          35

```

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<210> 42
<211> 1305
<212> DNA
<213> Streptococcus

```

```

<400> 42
atgaaaatga ataaaaaggt actattgaca tcgacaatgg cagcttcgct attatcagtc      60
gcaagtgttc aagcacaaga aacagatacg acgtggacag cacgtactgt ttcagaggta      120
aaggctgatt tggtaaagca agacaataaa tcatcatata ctgtgaaata tggtgatata      180
ctaagcgtaa tttcagaagc aatgtcaatt gatatgaatg tcttagcaaa aattaataac      240
attgcagata tcaatcttat ttatcctgag acaacactga cagtaactta cgatcagaag      300
agtcatactg ccacttcaat gaaaatagaa acaccagcaa caaatgctgc tgggtcaaaca      360

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62 / 63

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acagctactg tggatttgaa aaccaatcaa gtttctgttg cagacccaaa agtttctctc 420
aatacaattt cggaaggtat gacaccagaa gcagcaacaa cgattgtttc gccaatgaag 480
acatatcttt ctgcgccagc tttgaaatca aaagaagtat tagcacaaga gcaagctggt 540
agtcaagcag cagctaataga acaggtatca acagctcctg tgaagtcgat tacttcagaa 600
gttccagcag cttaaagagga agttaaacca actcagacgt cagtcagtca gtcaacaaca 660
gtatcaccag cttctgttgc cgctgaaaca ccagctccag tagctaaagt agcaccggtg 720
agaactgtag cagcccctag agtggcaagt gttaaagtag tcactcctaa agtagaaact 780
ggtgcatcac cagagcatgt atcagctcca gcagttcctg tgactacgac ttcaacagct 840
acagacagta agttacaagc gactgaagtt aagagcgctc cggtagcaca aaaagctcca 900
acagcaacac cggtagcaca accagcttca acaacaaatg cagtagctgc acatcctgaa 960
aatgcagggc tccaacctca tgttgcagct tataaagaaa aagtagcgct aacttatgga 1020
gttaaatgaat tcagtacata ccgtgcaggt gatccaggtg atcatggtaa aggttttagca 1080
gtcgacttta ttgtaggtaa aaaccaagca cttggtaatg aagttgcaca gtactctaca 1140
caaaatatgg cagcaaataa catttcatat gttatctggc aacaaaagtt ttactcaaat 1200
acaaatagta tttatggacc tgctaatact tggaatgcaa tgccagatcg tgggtggcgtt 1260
actgcccaacc attatgacca tgttcacgta tcatttaaca aataa 1305

```

<210> 43

<211> 1230

<212> DNA

<213> Streptococcus

<400> 43

```

caagaaacag atacgacgtg gacagcacgt actgtttcag aggtaaaggc tgatttggtg 60
aagcaagaca ataaatcatc atatactgtg aaatatgggtg atacactaag cgttatttca 120
gaagcaatgt caattgatat gaatgtctta gcaaaaatta ataacattgc agatatcaat 180
cttattttatc ctgagacaac actgacagta acttacgac agagagtgca tactgccact 240
tcaatgaaaa tagaaacacc agcaacaaat gctgctggtc aaacaacagc tactgtggat 300
ttgaaaacca atcaagtttc tgttgcagac caaaaagttt ctctcaatac aatttcggaa 360
ggtatgacac cagaagcagc aacaacgatt gtttcgccaa tgaagacata ttcttctgcg 420
ccagctttga aatcaaaaaga agtattagca caagagcaag ctgttagtca agcagcagct 480
aatgaacagg tatcaacagc tcctgtgaag tcgattactt cagaagttcc agcagctaaa 540
gaggaagtta aaccaactca gacgtcagtc agtcagtcaa caacagtatc accagcttct 600
gttgccgctg aaacaccagc tccagtagct aaagtagcac cggtaagaac tgtagcagcc 660
cctagagtgg caagtgttaa agtagtcact cctaaagtag aaactgggtg atcaccagag 720
catgtatcag ctccagcagt tcctgtgact acgacttcaa cagctacaga cagtaagtta 780
caagcgactg aagttaagag cgttccggta gcacaaaaag ctccaacagc aacaccggta 840
gcacaaccag cttcaacaac aaatgcagta gctgcacatc ctgaaaatgc agggctccaa 900
cctcatgttg cagcttataa agaaaaagta gcgtaactt atggagttaa tgaattcagt 960
acataccgtg caggtgatcc aggtgatcat ggtaaagggt tagcagtcga ctttattgta 1020
ggtaaaaacc aagcacttgg taatgaagtt gcacagtact ctacacaaaa tatggcagca 1080
aataacattt catatgttat ctggcaacaa aagttttact caaatacaaa tagtatttat 1140
ggacctgcta atacttggaa tgcaatgcca gatcgtgggtg gcgttactgc caaccattat 1200
gaccatgttc acgtatcatt taacaaataa 1230

```

<210> 44

<211> 409

<212> PRT

<213> Streptococcus

<400> 44

```

Gln Glu Thr Asp Thr Thr Trp Thr Ala Arg Thr Val Ser Glu Val Lys
 1             5             10             15
Ala Asp Leu Val Lys Gln Asp Asn Lys Ser Ser Tyr Thr Val Lys Tyr
      20             25             30
Gly Asp Thr Leu Ser Val Ile Ser Glu Ala Met Ser Ile Asp Met Asn

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